

10/590724

***** INVENTOR RESULTS *****

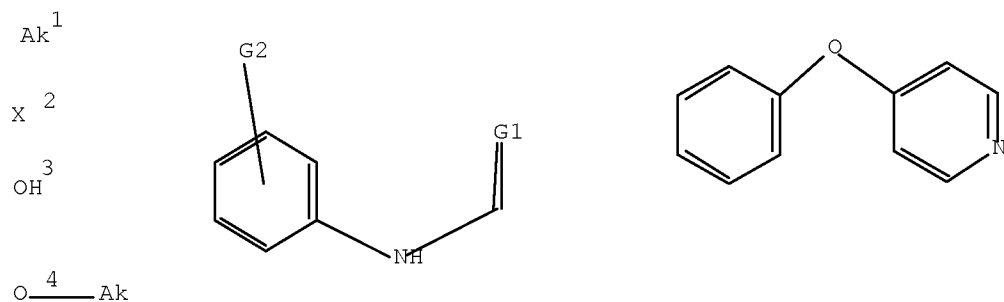
=> d his 178

(FILE 'HCAPLUS' ENTERED AT 13:24:34 ON 16 JUL 2008)

L78 5 S L77 NOT L54

=> d que 178

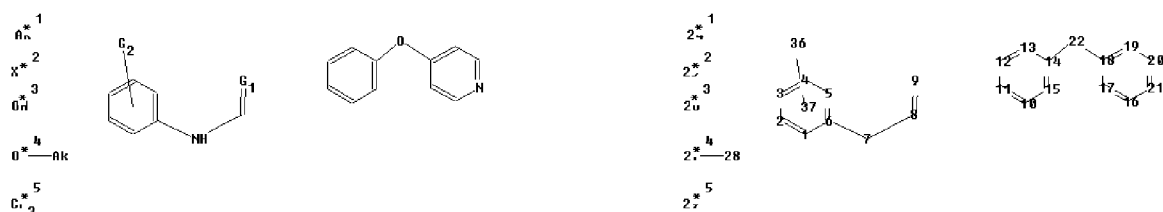
L1 1 SEA FILE=HCAPLUS ABB=ON PLU=ON US20070142440/PN
L47 STR



CF₃⁵
G1 O,S
G2 [01],[02],[03],[04],[05]

Structure attributes must be viewed using STN Express query preparation:

Uploading L11.str



chain nodes :

7 8 9 22 24 25 26 27 28 29 36

ring nodes :

1 2 3 4 5 6 10 11 12 13 14 15 16 17 18 19 20 21

chain bonds :

6-7 7-8 8-9 14-22 18-22 27-28

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21

17-18 18-19 19-20 20-21

exact/norm bonds :

6-7 7-8 8-9 14-22 18-22 27-28

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normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21
17-18 18-19 19-20 20-21

isolated ring systems :

containing 1 : 10 : 16 :

G1:O,S

G2:[*1],[*2],[*3],[*4],[*5]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom
22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 36:CLASS
37:Atom

L48 SCR 2043 AND 1918 AND 2050
L50 1662 SEA FILE=REGISTRY SSS FUL L47 NOT L48
L52 607 SEA FILE=HCAPLUS ABB=ON PLU=ON L50
L53 584 SEA FILE=HCAPLUS ABB=ON PLU=ON L52 AND PHARMAC?/SC,SX
L54 64 SEA FILE=HCAPLUS ABB=ON PLU=ON L53 AND (AY<2004 OR PY<2004
OR PRY<2004)
L69 22 SEA FILE=HCAPLUS ABB=ON PLU=ON BURGDORF L?/AU
L70 45 SEA FILE=HCAPLUS ABB=ON PLU=ON BUCHSTALLER H?/AU
L71 36 SEA FILE=HCAPLUS ABB=ON PLU=ON STIEBER F?/AU
L72 28 SEA FILE=HCAPLUS ABB=ON PLU=ON AMENDT C?/AU
L73 202 SEA FILE=HCAPLUS ABB=ON PLU=ON GREINER H?/AU
L74 150 SEA FILE=HCAPLUS ABB=ON PLU=ON GRELL M?/AU
L75 38 SEA FILE=HCAPLUS ABB=ON PLU=ON SIRRENBURG C?/AU
L76 3 SEA FILE=HCAPLUS ABB=ON PLU=ON ZENKE K?/AU
L77 10 SEA FILE=HCAPLUS ABB=ON PLU=ON (((L69 OR L70 OR L71 OR L72
OR L73 OR L74 OR L75 OR L76)) AND L52) OR (L1 AND L52)
L78 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L77 NOT L54

=> d his 1107

(FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 13:48:43 ON 16 JUL 2008)
L107 3 S (L100-L106) AND TYROSINE KINASE?

=> d que 1107

L100 9 SEA BUCHSTALLER HANS PETER/AU
L101 8 SEA STIEBER FRANK/AU
L102 7 SEA AMENDT CHRISTIANE/AU
L103 14 SEA GREINER HARTMUT/AU
L104 70 SEA GRELL MATTHIAS/AU
L105 19 SEA SIRRENBURG CHRISTIAN/AU
L106 2 SEA ZENKE FRANK/AU
L107 3 SEA ((L100 OR L101 OR L102 OR L103 OR L104 OR L105 OR L106))
AND TYROSINE KINASE?

=> dup rem 178 1107

FILE 'HCAPLUS' ENTERED AT 13:53:35 ON 16 JUL 2008

10/590724

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'MEDLINE' ENTERED AT 13:53:35 ON 16 JUL 2008

FILE 'EMBASE' ENTERED AT 13:53:35 ON 16 JUL 2008

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PROCESSING COMPLETED FOR L78

PROCESSING COMPLETED FOR L107

L109 8 DUP REM L78 L107 (0 DUPLICATES REMOVED)

ANSWERS '1-5' FROM FILE HCAPLUS

ANSWERS '6-7' FROM FILE MEDLINE

ANSWER '8' FROM FILE EMBASE

=> d l109 1-5 ibib abs; d l109 6-8 ibib ab

L109 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:817202 HCAPLUS Full-text

DOCUMENT NUMBER: 147:158473

TITLE: Use of integrin ligands and co-therapeutic agents for isolated organ perfusion combination therapy of cancer

INVENTOR(S): Goodman, Simon; Grell, Matthias; Ten Hagen, Timo L. M.; Egermont, Alexander M. M.

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 54pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2007082742 | A1 | 20070726 | WO 2007-EP408 | 20070118 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |

PRIORITY APPLN. INFO.: EP 2006-1049 A 20060118

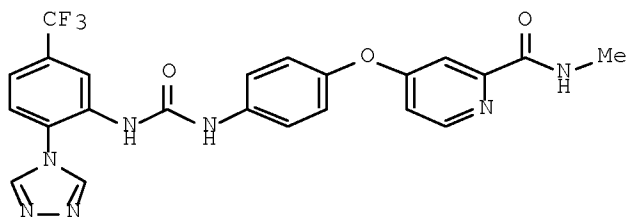
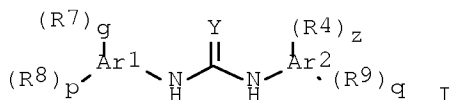
AB The invention discloses a combination therapy for the treatment of tumors and tumor metastases comprising administration of integrin ligands, preferably integrin antagonists, together with co-therapeutic agents or therapy forms that have synergistic efficacy when administered together with the ligands, such as chemotherapeutic agents and/or radiation therapy, in isolated organ perfusion. The therapy results in a synergistic potential increase of the inhibition effect of each individual therapeutic on tumor cell proliferation, yielding more effective treatment than found by administering an individual component alone.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/590724

L109 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2006:364321 HCAPLUS Full-text
 DOCUMENT NUMBER: 144:412515
 TITLE: Heterocyclic substituted bisarylurea derivatives as
 kinase inhibitors and their preparation,
 pharmaceutical compositions, and use for treatment of
 diseases mediated or propagated by kinases
 INVENTOR(S): Stieber, Frank; Jonczyk, Alfred; Hoelzemann,
 Guenter; Buchstaller, Hans-Peter;
 Burgdorf, Lars Thore; Rautenberg, Wilfried;
 Greiner, Hartmut
 PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
 SOURCE: PCT Int. Appl., 232 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|------------|
| WO 2006040056 | A1 | 20060420 | WO 2005-EP10744 | 20051006 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| AU 2005293839 | A1 | 20060420 | AU 2005-293839 | 20051006 |
| CA 2584185 | A1 | 20060420 | CA 2005-2584185 | 20051006 |
| EP 1799669 | A1 | 20070627 | EP 2005-789864 | 20051006 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |
| CN 101039932 | A | 20070919 | CN 2005-80035117 | 20051006 |
| JP 2008515943 | T | 20080515 | JP 2007-536047 | 20051006 |
| MX 200704248 | A | 20070612 | MX 2007-4248 | 20070410 |
| KR 2007062998 | A | 20070618 | KR 2007-708364 | 20070412 |
| IN 2007KN01680 | A | 20070727 | IN 2007-KN1680 | 20070511 |
| PRIORITY APPLN. INFO.: | | | EP 2004-24369 | A 20041013 |
| | | | EP 2005-16845 | A 20050803 |
| | | | WO 2005-EP10744 | W 20051006 |
| OTHER SOURCE(S): | | | MARPAT 144:412515 | |
| GI | | | | |



II

AB The invention relates to heterocyclic substituted bisarylurea derivs. of formula I, the use of the compds. of formula I as inhibitors of one or more kinases, the use of the compds. of formula I for the manufacture of a pharmaceutical composition and a method of treatment, comprising administering said pharmaceutical composition to a patient. Compds. of formula I wherein R4 is (X-Ar3) α -(R10) λ ; Ar1, Ar2, and Ar3 are independently 5- to 14-membered unsatd. or aromatic cyclic hydrocarbon, or 2- to 10-membered unsatd. or aromatic heterocyclic residue, preferably 1 to 5 heteroatoms selected from N, O, and S; α is 0, 1, or 2; r, z, and p are independently 0, 1, 2, 3, 4 or 5; R7 is nitrogen containing heterocyclic moiety bound directly to Ar1 via a nitrogen atom, etc.; R8, R9, and R10 are independently H, (alkoxy)alkyl, alkenyl, C3-7 cycloalkyl, alkenylcycloalkyl, halo, CH2halo, CH(halo)2, C(halo)3, NO2, etc.; Y is O, S, NH and derivs., (un)substituted CHNO2, (un)substituted CHCN, or C(CN)2; g is 1, 2, or 3; q is 0, 1, 2, 3 or 4; and their pharmaceutically acceptable derivs., salts and solvates thereof are claimed in this invention. Example compound II was prepared by chlorination and esterification of pyridine-2-carboxylic acid to give Me 4-chloropyridine-2-carboxylate, which underwent amidation with methylamine to give 4-chloropyridine-2-carboxylic acid methylamide, which was reacted with 4-aminophenol; the resulting 4-(4-aminophenoxy)pyridine-2-carboxylic acid methylamine reacted with p-nitrophenyl chloroformate and 4-(2-amino-4-trifluoromethylphenyl)-1,2,4-triazole to give example compound II. All the invention compds. were evaluated for their activity as modulators and inhibitors of kinases. From the assay, it was determined that these compds. preferably inhibit VEGF-stimulated mitogenesis of human vascular endothelial cells in cultures with IC50 values of 0.01-5.0 μ M.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L109 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:977019 HCAPLUS Full-text

DOCUMENT NUMBER: 143:286162

TITLE: Preparation of aryl semicarbazide derivatives as kinase inhibitors

INVENTOR(S): Buchstaller, Hans-Peter; Finsinger, Dirk; Stieber, Frank; Wiesner, Matthias; Amendt, Christiane; Sirrenberg, Christian; Zenke, Frank; Grell, Matthias

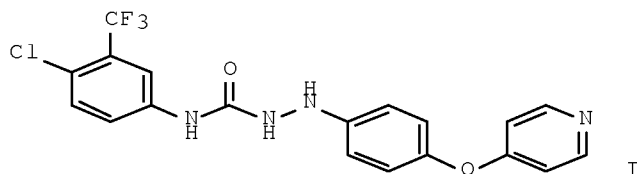
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 278 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2005082853 | A1 | 20050909 | WO 2005-EP1443 | 20050214 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2005217041 | A1 | 20050909 | AU 2005-217041 | 20050214 |
| CA 2557359 | A1 | 20050909 | CA 2005-2557359 | 20050214 |
| EP 1727800 | A1 | 20061206 | EP 2005-715319 | 20050214 |
| R: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | |
| JP 2007523928 | T | 20070823 | JP 2007-500096 | 20050214 |
| PRIORITY APPLN. INFO.: | | | EP 2004-4330 | A 20040226 |
| | | | WO 2005-EP1443 | W 20050214 |
| OTHER SOURCE(S): | CASREACT 143:286162; MARPAT 143:286162 | | | |
| GI | | | | |



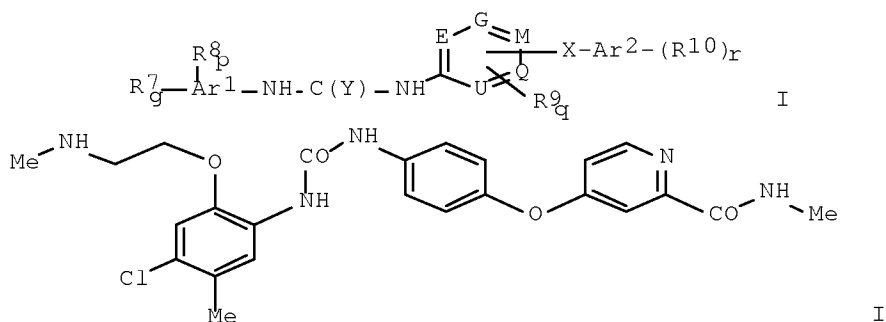
AB Title compds. of formula A-D-B [D = bivalent semicarbazide moiety, or a derivative thereof; A = (un)substituted moiety L-(M-L1)_n where L = 5-7 membered cyclic structure, preferably selected from the group consisting of aryl, heteroaryl, arylene, and heteroarylene, bound directly to D, L1 = (un)substituted cyclic moiety preferably selected from aryl, heteroaryl, aralkyl, cycloalkyl, and heterocyclyl, M = bond or bridging group, n = 0-4; B = (un)substituted, up to tricyclic aryl or heteroaryl moiety], and their pharmaceutically acceptable salts are prepared and disclosed as inhibitors of one or more kinases (no data). Thus, e.g., I was prepared by reaction of 4-chloro-3-trifluoromethylphenyl isocyanate with 4-(pyridin-4-yloxy)phenylhydrazine (preparation given). Further disclosures include the use of the compds. of the invention for the manufacture of a pharmaceutical composition and a method of treatment, comprising administering said pharmaceutical composition to a patient.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/590724

L109 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2005:823661 HCAPLUS Full-text
 DOCUMENT NUMBER: 143:229726
 TITLE: Preparation of 1,3-diaryllureas as inhibitors of raf
 and other kinases useful against cancer and other
 diseases
 INVENTOR(S): Buchstaller, Hans-Peter; Burgdorf,
 Lars; Stieber, Frank; Amendt,
 Christiane; Grell, Matthias;
 Sirrenberg, Christian; Zenke, Frank
 PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
 SOURCE: PCT Int. Appl., 264 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|-------------------|------------------|------------|
| WO 2005075425 | A2 | 20050818 | WO 2005-EP387 | 20050117 |
| WO 2005075425 | A3 | 20061214 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2005211448 | A1 | 20050818 | AU 2005-211448 | 20050117 |
| CA 2554878 | A1 | 20050818 | CA 2005-2554878 | 20050117 |
| EP 1730111 | A2 | 20061213 | EP 2005-700967 | 20050117 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU | | | | |
| CN 1972925 | A | 20070530 | CN 2005-80002901 | 20050117 |
| BR 2005007198 | A | 20070626 | BR 2005-7198 | 20050117 |
| JP 2007519653 | T | 20070719 | JP 2006-549997 | 20050117 |
| US 20070161677 | A1 | 20070712 | US 2006-587292 | 20060725 |
| MX 2006PA08449 | A | 20061002 | MX 2006-PA8449 | 20060726 |
| IN 2006KN02441 | A | 20070525 | IN 2006-KN2441 | 20060828 |
| PRIORITY APPLN. INFO.: | | | EP 2004-2092 | A 20040130 |
| | | | WO 2005-EP387 | W 20050117 |
| OTHER SOURCE(S): | | MARPAT 143:229726 | | |
| GI | | | | |



AB The present invention relates to bisarylurea derivs. (shown as I; variables defined below; e.g. 4-[4-[3-[4-chloro-5-methyl-2-(2-methylaminoethoxy)phenyl]ureido]phenoxy]pyridine-2-carboxylic acid methylamide (shown as II)), their use as inhibitors of raf-kinase (no data) and for the manufacture of a pharmaceutical composition and a method of treatment, comprising administering said pharmaceutical composition to a patient. Methods of preparation are claimed and >100 example preps. are included. For example, 1-[2-[2-[(tert-butoxycarbonyl)(methyl)amino]ethoxy]-5-(trifluoromethyl)phenyl]-3-[4-[[2-(methylcarbamoyl)pyridin-4-yl]oxy]phenyl]urea was prepared (87 %) by reacting tert-Bu [2-[2-amino-4-(trifluoromethyl)phenoxy]ethyl](methyl)carbamate (preparation given) with p-nitrophenyl chloroformate followed by N-methyl-4-(4-aminophenoxy)pyridine-2-carboxamide (preparation given) and DIPEA; deprotection gave 86 % 1-[2-[2-(methylamino)ethoxy]-5-(trifluoromethyl)phenyl]-3-[4-[[2-(methylcarbamoyl)pyridin-4-yl]oxy]phenyl]urea. For I: Ar1, Ar2 = aromatic hydrocarbons containing 6 to 14 C atoms and ethylenic unsatd. or aromatic heterocyclic residues containing 3 to 10 C atoms and one or two heteroatoms, = N, O and S; E, G, M, Q and U = C and N atoms, with the proviso that ≥ 1 of E, G, M, Q and U are C atoms and that X is bonded to a C atom. R7 = Het, OHet, N(R11)Het, (CR5R6)kHet, et al. or R7 = -SO2-CR8:CR8-, wherein both valencies are bound vicinally to Ar1; R8, R9 and R10 = H, A, cycloalkyl comprising 3 to 7 C atoms, Hal, et al.; Y = O, S, NR21, C(R22)-NO2, C(R22)-CN and C(CN)2; g = 1-3, preferably 1 or 2, p, r = 0-5; q = 0-4, preferably 0, 1 or 2; addnl. details are given in the claims.

L109 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:982303 HCAPLUS Full-text

DOCUMENT NUMBER: 143:286291

TITLE: Preparation of 2-pyridinecarboxamides as kinase inhibitors

INVENTOR(S): Burgorf, Lars; Buchstaller, Hans-Peter;
Stieber, Frank; Amendt, Christiane;
Greiner, Hartmut; Grell, Matthias;
Sirrenberg, Christian; Zenke, Frank

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: Ger. Offen., 33 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

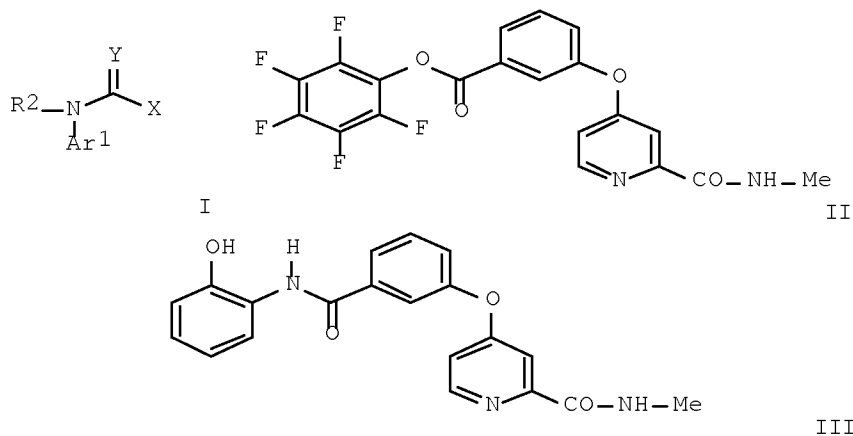
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

10/590724

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-------------------|-----------------------|--------------|
| DE 102004009238 | A1 | 20050908 | DE 2004-102004009238 | 20040226 |
| AU 2005219496 | A1 | 20050915 | AU 2005-219496 | 20050113 |
| CA 2557302 | A1 | 20050915 | CA 2005-2557302 | 20050113 |
| WO 2005085202 | A1 | 20050915 | WO 2005-EP273 | 20050113 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1718614 | A1 | 20061108 | EP 2005-700886 | 20050113 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS | | | | |
| JP 2007523921 | T | 20070823 | JP 2007-500077 | 20050113 |
| US 20070142440 | A1 | 20070621 | US 2006-590724 | 20060825 <-- |
| PRIORITY APPLN. INFO.: | | | DE 2004-102004009238A | 20040226 |
| | | | WO 2005-EP273 | W 20050113 |
| OTHER SOURCE(S): | | MARPAT 143:286291 | | |
| GI | | | | |



AB Title compds. I [X = Ar₂-Z-Ar₃; Ar₁, Ar₂, Ar₃ = (un)substituted aromatic, het; R₁ = H, aryl, O-aryl, etc.; R₂ = H, A, alkylene-aryl, etc.; A = alkyl with provisos; Z = Gln, GlnEG₂m, EGlnG₂m, etc.; E = O, CO, C=N, etc.; G₁, G₂ = CR₁R₁, E; n = 0-5; m = 0-2] and their pharmaceutically acceptable salts and formulations were prepared. For example, N-alkylation of 2-aminophenol with pentafluorophenol II afforded pyridinecarboxamide III in 13% yield. Compds. I are claimed to be effective inhibitors of the tyrosine kinases, in particular TIE-2 and VEGFR, and the Raf kinases.

L109 ANSWER 6 OF 8 MEDLINE on STN
 ACCESSION NUMBER: 2003332773 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 12866072
 TITLE: Multistep solid-phase synthesis of an antibiotic and
 receptor tyrosine kinase inhibitors
 using the traceless phenylhydrazide linker.
 AUTHOR: Stieber Frank; Grether Uwe; Mazitschek Ralph;
 Soric Natascha; Giannis Athanassios; Waldmann Herbert
 CORPORATE SOURCE: Max-Planck-Institut fur Molekulare Physiologie, Abteilung
 Chemische Biologie, Otto-Hahn-Strasse 11, 44227 Dortmund,
 Germany.
 SOURCE: Chemistry (Weinheim an der Bergstrasse, Germany), (2003 Jul
 21) Vol. 9, No. 14, pp. 3282-91.
 Journal code: 9513783. ISSN: 0947-6539.
 PUB. COUNTRY: Germany: Germany, Federal Republic of
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200309
 ENTRY DATE: Entered STN: 17 Jul 2003
 Last Updated on STN: 11 Sep 2003
 Entered Medline: 10 Sep 2003

AB The hydrazide group is an oxidatively cleavable traceless linker for solid-
 phase chemistry. This linker technology was used to develop a multistep
 solid-phase synthesis of an antibiotic that is active against Mycobacterium
 tuberculosis. Furthermore, we describe an efficient method for the traceless
 synthesis of 2-aminothiazoles that display dual inhibitory activity against
 the receptor tyrosine kinases VEGFR-2 and Tie-2. The synthesis method
 proceeds through 9 steps on the solid phase and should give access to a much
 larger library of 2-aminothiazoles, from which a new class of anti-
 angiogenesis drugs may be developed.

L109 ANSWER 7 OF 8 MEDLINE on STN
 ACCESSION NUMBER: 2003043368 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 12481350
 TITLE: Traceless solid-phase synthesis of 2-aminothiazoles:
 receptor tyrosine kinase inhibitors
 with dual selectivity for Tie-2 and VEGFR-2.
 AUTHOR: Stieber Frank; Mazitschek Ralph; Soric Natascha;
 Giannis Athanassios; Waldmann Herbert
 CORPORATE SOURCE: Max-Planck-Institut fur molekulare Physiologie, Abteilung
 Chemische Biologie, Otto-Hahn-Strasse 11, 44227 Dortmund,
 Germany.
 SOURCE: Angewandte Chemie (International ed. in English), (2002 Dec
 16) Vol. 41, No. 24, pp. 4757-61.
 Journal code: 0370543. ISSN: 1433-7851.
 PUB. COUNTRY: Germany: Germany, Federal Republic of
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200303

10/590724

ENTRY DATE: Entered STN: 30 Jan 2003
Last Updated on STN: 19 Mar 2003
Entered Medline: 18 Mar 2003

L109 ANSWER 8 OF 8 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1996270766 EMBASE Full-text
TITLE: Neurotrophins stimulate the release of dopamine from rat mesencephalic neurons via Trk and p75(Lntr) receptors.
AUTHOR: Blochl, Andrea (correspondence); Sirrenberg, Christian
CORPORATE SOURCE: Max-Planck-Institute for Psychiatry, Department of Neurochemistry, D-82152 Martinsried, Germany. Bloechl@alf.biochem.mpg.de
AUTHOR: Blochl, Andrea (correspondence)
CORPORATE SOURCE: Max-Planck-Institute for Psychiatry, Dept. of Neurochemistry, Am Klopferspitz 18a, D-82152 Martinsried, Germany. Bloechl@alf.biochem.mpg.de
AUTHOR: Sirrenberg, Christian
CORPORATE SOURCE: Ludwig-Maximilian-University Munich, Dept. of Biochemistry, 80336 Munich, Germany.
AUTHOR: Blochl, Andrea (correspondence)
CORPORATE SOURCE: Dept. of Neurochemistry, Max-Planck-Institute for Psychiatry, Am Klopferspitz 18a, D-82152 Martinsried, Germany.
SOURCE: Journal of Biological Chemistry, (1996) Vol. 271, No. 35, pp. 21100-21107.
Refs: 64
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical and Experimental Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 7 Oct 1996
Last Updated on STN: 7 Oct 1996

AB We analyzed the short term effect of neurotrophins on mesencephalic neuronal cultures of embryonic (E14) rats with respect to which receptors mediate the actions. Brain-derived neurotrophic factor (BDNF) or neurotrophin-3 enhanced within minutes in a dose-dependent manner (2, 20, 100 ng/ml for 5 min) depolarization-induced (KCl, 30 mM 5 min) and basal dopamine release, but nerve growth factor (NGF) was only effective at high doses (100 ng/ml). The effect of BDNF, but not of NGF, was blocked by K252a or K252b. BDNF, but not NGF, phosphorylated trkB receptors. The NGF-induced, but not the BDNF-induced effect upon the release of dopamine was blocked by anti-p75 antibody MC192. C(2)-ceramide, an analogue of ceramide, the second messenger of the sphingomyelin pathway, and sphingomyelinase itself induced a release of dopamine comparable with the effect of NGF. NGF, but not BDNF, increased ceramide production. In addition, simultaneous treatment with BDNF and NGF led to a partial prevention of the NGF stimulated, p75(Lntr)-mediated effect. We conclude that BDNF stimulates the release of dopamine by activation of the trkB receptor, whereas NGF affects the release via the p75(Lntr) receptor inducing the sphingomyelin pathway.

10/590724

***** QUERY RESULTS *****

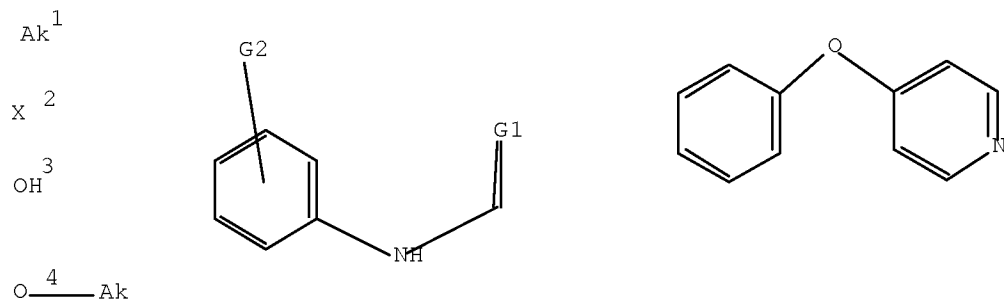
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L54 64 S L53 AND (AY<2004 OR PY<2004 OR PRY<2004)

=> d que 154

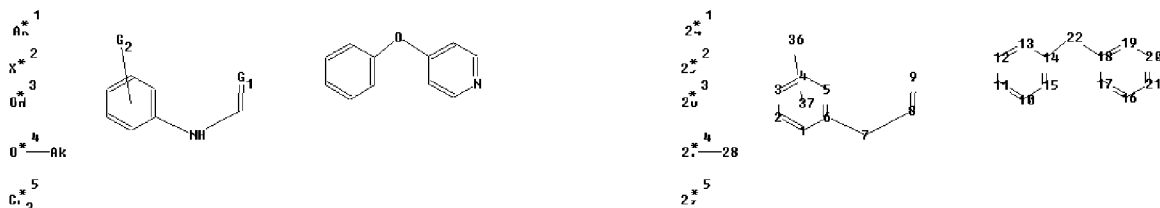
L47 STR



CF₃⁵
G1 O,S
G2 [01],[02],[03],[04],[05]

Structure attributes must be viewed using STN Express query preparation:

Uploading L11.str



chain nodes :

7 8 9 22 24 25 26 27 28 29 36

ring nodes :

1 2 3 4 5 6 10 11 12 13 14 15 16 17 18 19 20 21

chain bonds :

6-7 7-8 8-9 14-22 18-22 27-28

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21

17-18 18-19 19-20 20-21

exact/norm bonds :

10/590724

6-7 7-8 8-9 14-22 18-22 27-28

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21

17-18 18-19 19-20 20-21

isolated ring systems :

containing 1 : 10 : 16 :

G1:O,S

G2:[*1],[*2],[*3],[*4],[*5]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom

11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom

20:Atom 21:Atom

22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 36:CLASS

37:Atom

L48 SCR 2043 AND 1918 AND 2050

L50 1662 SEA FILE=REGISTRY SSS FUL L47 NOT L48

L52 607 SEA FILE=HCAPLUS ABB=ON PLU=ON L50

L53 584 SEA FILE=HCAPLUS ABB=ON PLU=ON L52 AND PHARMAC?/SC,SX

L54 64 SEA FILE=HCAPLUS ABB=ON PLU=ON L53 AND (AY<2004 OR PY<2004 OR PRY<2004)

=> d his 186

(FILE 'BIOSIS' ENTERED AT 13:39:15 ON 16 JUL 2008)

L86 8 S L83 OR L85

=> d que 186

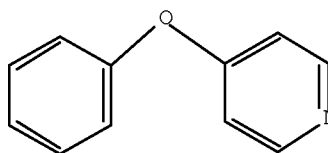
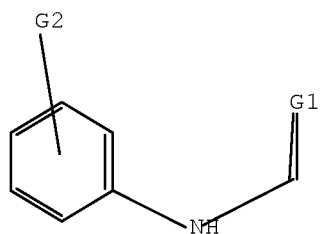
L47 STR

Ak¹

X²

OH³

O⁴ Ak



CF₃⁵

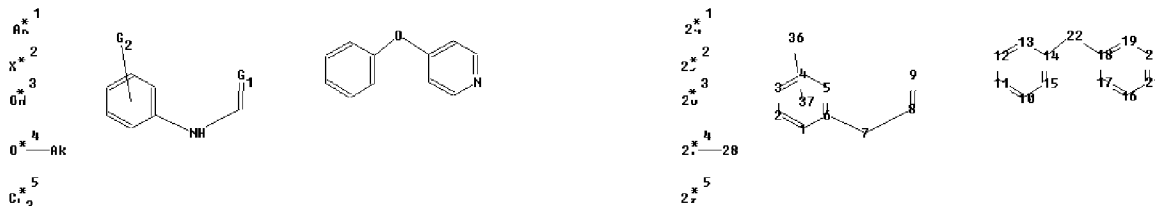
G1 O,S

G2 [@1],[@2],[@3],[@4],[@5]

10/590724

Structure attributes must be viewed using STN Express query preparation:

Uploading L11.str



chain nodes :
7 8 9 22 24 25 26 27 28 29 36
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15 16 17 18 19 20 21
chain bonds :
6-7 7-8 8-9 14-22 18-22 27-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21
17-18 18-19 19-20 20-21
exact/norm bonds :
6-7 7-8 8-9 14-22 18-22 27-28
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21
17-18 18-19 19-20 20-21
isolated ring systems :
containing 1 : 10 : 16 :

G1:O,S

G2:[*1],[*2],[*3],[*4],[*5]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom
22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 36:CLASS
37:Atom

L48 SCR 2043 AND 1918 AND 2050
L50 1662 SEA FILE=REGISTRY SSS FUL L47 NOT L48
L64 1797 SEA FILE=HCAPLUS ABB=ON PLU=ON (TIE2 OR TIE(W)2 OR VEGFR OR
RAF) (W) (KINASE? OR KINASE INHIB?)
L79 1 SEA FILE=REGISTRY ABB=ON PLU=ON L50 AND (MEDLINE/LC OR
BIOSIS/LC OR DRUGU/LC OR EMBASE/LC)
L81 89 SEA FILE=BIOSIS ABB=ON PLU=ON L79
L82 34 SEA FILE=BIOSIS ABB=ON PLU=ON L81 AND L64

10/590724

L83 3 SEA FILE=BIOSIS ABB=ON PLU=ON L82 AND (PREP? OR SYNTHES?)
 L85 6 SEA FILE=BIOSIS ABB=ON PLU=ON L82 AND TYROSINE KINASE?
 L86 8 SEA FILE=BIOSIS ABB=ON PLU=ON L83 OR L85

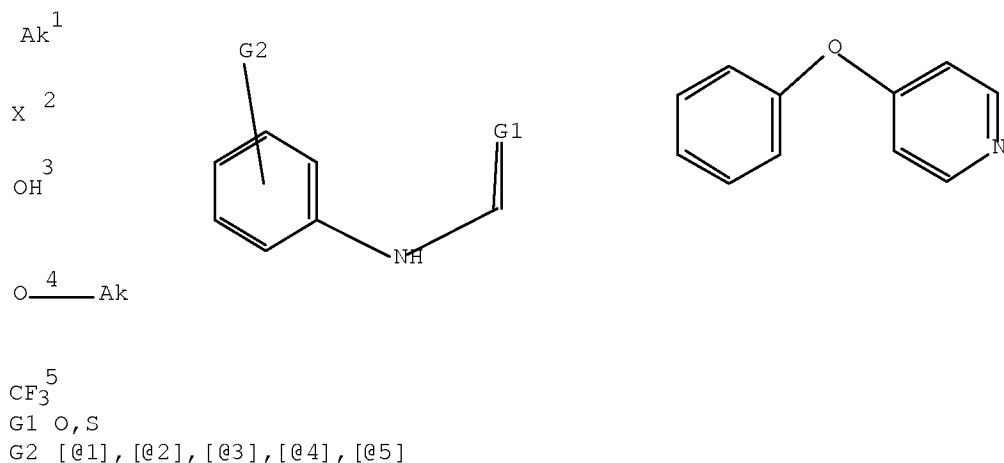
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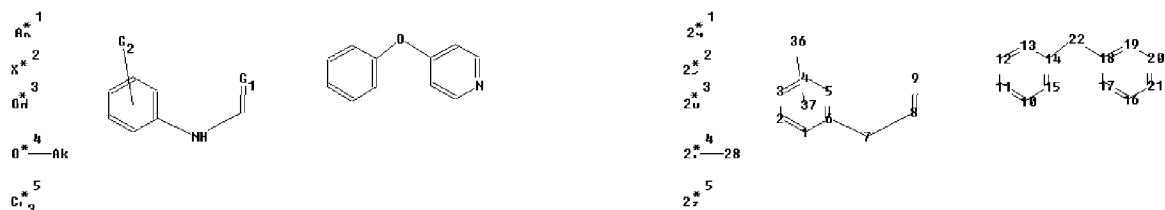
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L47 STR



Structure attributes must be viewed using STN Express query preparation:

Uploading L11.str



chain nodes :

7 8 9 22 24 25 26 27 28 29 36

ring nodes :

1 2 3 4 5 6 10 11 12 13 14 15 16 17 18 19 20 21

chain bonds :

6-7 7-8 8-9 14-22 18-22 27-28

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-

21
 17-18 18-19 19-20 20-21
 exact/norm bonds :
 6-7 7-8 8-9 14-22 18-22 27-28
 normalized bonds :
 1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21
 17-18 18-19 19-20 20-21
 isolated ring systems :
 containing 1 : 10 : 16 :

G1:O,S

G2:[*1],[*2],[*3],[*4],[*5]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom
 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
 20:Atom 21:Atom
 22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 36:CLASS
 37:Atom

L48 SCR 2043 AND 1918 AND 2050
 L50 1662 SEA FILE=REGISTRY SSS FUL L47 NOT L48
 L79 1 SEA FILE=REGISTRY ABB=ON PLU=ON L50 AND (MEDLINE/LC OR
 BIOSIS/LC OR DRUGU/LC OR EMBASE/LC)
 L88 2050 SEA FILE=EMBASE ABB=ON PLU=ON L79
 L89 605 SEA FILE=EMBASE ABB=ON PLU=ON L88 AND TYROSINE KINASE?
 L98 12 SEA FILE=EMBASE ABB=ON PLU=ON L89 AND (AY<2004 OR PY<2004 OR
 PRY<2004)

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 PROCESSING COMPLETED FOR L54
 PROCESSING COMPLETED FOR L86
 PROCESSING COMPLETED FOR L98
 L110 84 DUP REM L54 L86 L98 (0 DUPLICATES REMOVED)
 ANSWERS '1-64' FROM FILE HCAPLUS
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 ANSWERS '73-84' FROM FILE EMBASE

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L110 ANSWER 1 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2007:863627 HCAPLUS Full-text
 DOCUMENT NUMBER: 147:235192

10/590724

TITLE: Preparation of urea derivatives containing nitrogenous aromatic ring compounds as inhibitors of angiogenesis

INVENTOR(S): Funahashi, Yasuhiro; Tsuruoka, Akihiko; Matsukura, Masayuki; Haneda, Toru; Fukuda, Yoshio; Kamata, Junichi; Takahashi, Keiko; Matsushima, Tomohiro; Miyazaki, Kazuki; Nomoto, Ken-Ichi; Watanabe, Tatsuo; Obaishi, Hiroshi; Yamaguchi, Atsumi; Suzuki, Sachi; Nakamura, Katsuji; Mimura, Fusayo; Yamamoto, Yuji; Matsui, Junji; Matsui, Kenji; Yoshida, Takako; Suzuki, Yasuyuki; Arimoto, Itaru

PATENT ASSIGNEE(S): Eisai Co., Ltd, Japan

SOURCE: U.S., 458pp., Cont.-in-part of Appl. No. PCT/JP01/09221.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

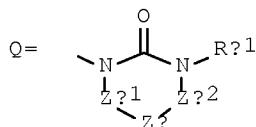
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| US 7253286 | B2 | 20070807 | US 2003-420466 | 20030418 <-- |
| US 20040053908 | A1 | 20040318 | | |
| WO 2002032872 | A1 | 20020425 | WO 2001-JP9221 | 20011019 <-- |
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| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
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| EP 1506962 | A3 | 20050302 | | |
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| CN 101029022 | A | 20070905 | CN 2007-10007097 | 20011019 <-- |
| ES 2282299 | T3 | 20071016 | ES 2001-976786 | 20011019 <-- |
| ZA 2003003567 | A | 20040810 | ZA 2003-3567 | 20030508 <-- |
| JP 2005272474 | A | 20051006 | JP 2005-124034 | 20050421 <-- |
| US 20060247259 | A1 | 20061102 | US 2005-293785 | 20051202 <-- |
| US 20060160832 | A1 | 20060720 | US 2006-347749 | 20060203 <-- |
| AU 2006203099 | A1 | 20060810 | AU 2006-203099 | 20060719 <-- |
| AU 2006236039 | A1 | 20061207 | AU 2006-236039 | 20061116 <-- |
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| PRIORITY APPLN. INFO.: | | | JP 2000-320420 | A 20001020 <-- |
| | | | JP 2000-386195 | A 20001220 <-- |
| | | | JP 2001-46685 | A 20010222 <-- |
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| | | | EP 2001-976786 | A3 20011019 <-- |
| | | | JP 2002-536056 | A3 20011019 <-- |

OTHER SOURCE(S):

MARPAT 147:235192

GI



AB N-aryl or N-heteroarylurea derivs. represented by the general formula Ag-Xg-Yg-Tgl or salts thereof, or hydrates of both [wherein Ag = (un)substituted C6-14 aryl or 5- to 14-membered heterocyclic group; Xg = single bond, O, S, C1-6 alkylene, SO, SO₂, (un)substituted NH; Yg = (un)substituted C6-14 aryl, 5- to 14-membered heterocyclic group, C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl-C1-6 alkyl, 5- to 14-membered heteroaryl-C1-6 alkyl, (CH₂)_gSO₂ (g = 1-8), (CH₂)_{fa}CH:CH(CH₂)_{fb} (fa, fb = 0, 1,2,3), etc.; and Tgl = a group of the general formula -Eg-CO-NR_{g1}(Z_g) or Q; wherein Eg = a single bond, (un)substituted NH; R_{g1} = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 aliphatic hydrocarbyl, etc.; Z_g = C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl, etc.; Z_{g1}, Z_{g2} = (a) a single bond, (b) C1-6 alkylene optionally having ≥1 atoms selected from O, S, and N in the middle or the terminus of the chain and optionally substituted with oxo, (c) (un)substituted C2-6 alkenyl] are prepared These compds. are also inhibitors of vascular endothelial growth factor receptor kinase (VEGFR2 kinase) and are useful as antitumor agents against hemangioma, pancreatic cancer, stomach cancer, colon cancer, breast cancer, prostate cancer, lung cancer, brain tumor, leukemia, or ovarian cancer, as cancer metastasis inhibitors, and for the treatment of retina neovascularization, diabetic retinopathy, atherosclerosis, or inflammatory diseases such as osteoarthritis, rheumatoid arthritis, psoriasis, or delayed hypersensitivity. Thus, to solution of 334 mg 4-[6-(4-benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenylamine in 4 mL DMF were added 0.066 mL pyridine and 0.102 mL Ph chlorocarbonate and stirred at room temperature for 2.5 h to give 330 mg N-[4-[6-(4-benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea which (260 mg) was hydrogenolyzed over platinum oxide in ethanol overnight to give 160 mg N-[4-[6-(4-hydroxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea (I). I showed IC₅₀ of 0.02 nM for inhibiting the vascular endothelial growth factor (VEGF)-stimulated sandwich tube formation in vascular endothelial cell.

IT 417714-74-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

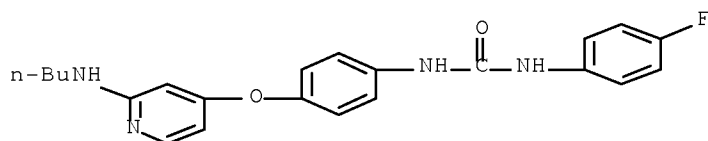
(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

RN 417714-74-0 HCAPLUS

CN Urea, N-[4-[[2-(butylamino)-4-pyridinyl]oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



INCL 546153000; 546155000; 514312000

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 27, 63

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| | 417712-91-5P | 417712-92-6P | 417712-93-7P | 417712-94-8P | 417712-95-9P |
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| | 417713-06-5P | 417713-08-7P | 417713-11-2P | 417713-12-3P | 417713-13-4P |
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| | 417713-51-0P | 417713-57-6P | 417713-59-8P | 417713-60-1P | 417713-62-3P |
| | 417713-63-4P | 417713-64-5P | 417713-65-6P | 417713-66-7P | 417713-67-8P |
| | 417713-68-9P | 417713-69-0P | 417713-70-3P | 417713-71-4P | 417713-75-8P |
| | 417713-76-9P | 417713-77-0P | 417713-84-9P | 417713-85-0P | 417713-87-2P |
| | 417713-90-7P | 417713-93-0P | 417713-94-1P | 417713-95-2P | 417713-96-3P |
| | 417713-97-4P | 417713-98-5P | 417713-99-6P | 417714-00-2P | 417714-01-3P |
| | 417714-02-4P | 417714-03-5P | 417714-05-7P | 417714-06-8P | 417714-07-9P |
| | 417714-08-0P | 417714-09-1P | 417714-11-5P | 417714-12-6P | 417714-14-8P |
| | 417714-15-9P | 417714-16-0P | 417714-17-1P | 417714-18-2P | 417714-19-3P |
| | 417714-20-6P | 417714-21-7P | 417714-22-8P | 417714-23-9P | 417714-24-0P |
| | 417714-25-1P | 417714-26-2P | 417714-27-3P | 417714-28-4P | 417714-29-5P |
| | 417714-30-8P | 417714-31-9P | 417714-32-0P | 417714-33-1P | 417714-36-4P |
| | 417714-37-5P | 417714-38-6P | 417714-39-7P | 417714-40-0P | 417714-41-1P |
| | 417714-42-2P | 417714-43-3P | 417714-44-4P | 417714-45-5P | 417714-46-6P |
| | 417714-47-7P | 417714-48-8P | 417714-49-9P | 417714-50-2P | 417714-51-3P |
| | 417714-52-4P | 417714-53-5P | 417714-54-6P | 417714-55-7P | 417714-58-0P |
| | 417714-59-1P | 417714-60-4P | 417714-62-6P | 417714-63-7P | 417714-64-8P |
| | 417714-65-9P | 417714-66-0P | 417714-67-1P | 417714-68-2P | 417714-69-3P |
| | 417714-70-6P | 417714-71-7P | 417714-72-8P | 417714-73-9P | |
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| | 417714-78-4P | 417714-79-5P | 417714-80-8P | 417714-81-9P | |
| | 417714-82-0P | 417714-83-1P | 417714-84-2P | 417714-85-3P | 417714-86-4P |
| | 417714-87-5P | 417714-89-7P | 417714-90-0P | 417714-91-1P | 417714-92-2P |
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| | 417714-97-7P | 417714-98-8P | 417714-99-9P | 417715-00-5P | |
| | 417715-01-6P | 417715-02-7P | 417715-03-8P | 417715-05-0P | 417715-07-2P |
| | 417715-08-3P | 417715-09-4P | 417715-10-7P | 417715-11-8P | 417715-12-9P |
| | 417715-13-0P | 417715-14-1P | 417715-15-2P | 417715-16-3P | 417715-17-4P |
| | 417715-18-5P | 417715-19-6P | 417715-20-9P | 417715-21-0P | 417715-22-1P |
| | 417715-23-2P | 417715-24-3P | 417715-25-4P | 417715-27-6P | 417715-28-7P |
| | 417715-29-8P | 417715-30-1P | 417715-31-2P | 417715-32-3P | 417715-33-4P |
| | 417715-34-5P | 417715-35-6P | 417715-36-7P | 417715-37-8P | 417715-39-0P |
| | 417715-40-3P | 417715-42-5P | 417715-44-7P | 417715-46-9P | 417715-47-0P |
| | 417715-49-2P | 417715-51-6P | 417715-53-8P | 417715-55-0P | 417715-57-2P |
| | 417715-59-4P | 417715-61-8P | 417715-63-0P | 417715-65-2P | 417715-66-3P |
| | 417715-67-4P | 417715-68-5P | 417715-69-6P | 417715-70-9P | |

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

| | | | | | |
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| IT | 417715-71-0P | 417715-72-1P | 417715-73-2P | 417715-74-3P | 417715-75-4P |
| | 417715-76-5P | 417715-77-6P | 417715-78-7P | 417715-79-8P | 417715-81-2P |
| | 417715-83-4P | 417715-85-6P | 417715-86-7P | 417715-88-9P | 417715-90-3P |
| | 417715-91-4P | 417715-93-6P | 417715-95-8P | 417715-97-0P | 417715-99-2P |
| | 417716-01-9P | 417716-03-1P | 417716-05-3P | 417716-06-4P | 417716-07-5P |
| | 417716-08-6P | 417716-09-7P | 417716-10-0P | 417716-12-2P | 417716-13-3P |
| | 417716-14-4P | 417716-15-5P | 417716-16-6P | 417716-17-7P | 417716-18-8P |
| | 417716-19-9P | 417716-20-2P | 417716-21-3P | 417716-22-4P | 417716-23-5P |
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| | 417716-29-1P | 417716-30-4P | 417716-31-5P | 417716-32-6P | 417716-33-7P |
| | 417716-34-8P | 417716-35-9P | 417716-36-0P | 417716-37-1P | 417716-38-2P |
| | 417716-39-3P | 417716-40-6P | 417716-41-7P | 417716-43-9P | 417716-44-0P |
| | 417716-45-1P | 417716-46-2P | 417716-47-3P | 417716-48-4P | 417716-49-5P |
| | 417716-50-8P | 417716-51-9P | 417716-52-0P | 417716-53-1P | 417716-54-2P |
| | 417716-55-3P | 417716-56-4P | 417716-57-5P | 417716-58-6P | 417716-59-7P |
| | 417716-60-0P | 417716-61-1P | 417716-62-2P | 417716-63-3P | 417716-64-4P |
| | 417716-65-5P | 417716-66-6P | 417716-67-7P | 417716-68-8P | 417716-69-9P |
| | 417716-70-2P | 417716-71-3P | 417716-72-4P | 417716-73-5P | 417716-74-6P |
| | 417716-75-7P | 417716-76-8P | 417716-77-9P | 417716-78-0P | 417716-79-1P |
| | 417716-80-4P | 417716-81-5P | 417716-82-6P | 417716-83-7P | 417716-84-8P |
| | 417716-85-9P | 417716-86-0P | 417716-87-1P | 417716-88-2P | 417716-89-3P |
| | 417716-90-6P | 417716-91-7P | 417716-92-8P | 417716-93-9P | 417716-94-0P |
| | 417716-95-1P | 417716-96-2P | 417716-97-3P | 417716-98-4P | 417716-99-5P |
| | 417717-00-1P | 417717-01-2P | 417717-02-3P | 417717-03-4P | 417717-04-5P |
| | 417717-05-6P | 417717-06-7P | 417717-07-8P | 417717-08-9P | 417717-09-0P |
| | 417717-10-3P | 417717-11-4P | 417717-14-7P | 417717-15-8P | 417717-16-9P |
| | 417717-17-0P | 417717-18-1P | 417717-19-2P | 417717-20-5P | 417717-22-7P |
| | 417717-23-8P | 417717-24-9P | 417717-25-0P | 417717-26-1P | 417717-27-2P |
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| | 417717-60-3P | 417717-62-5P | 417717-63-6P | 417717-64-7P | 417717-66-9P |
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| | 417717-77-2P | 417717-78-3P | 417717-79-4P | 417717-81-8P | 417717-83-0P |
| | 417717-86-3P | 417717-87-4P | 417717-88-5P | 417717-89-6P | 417717-93-2P |
| | 417717-95-4P | 417717-97-6P | 417717-99-8P | 417718-00-4P | 417718-02-6P |
| | 417718-04-8P | 417718-06-0P | 417718-10-6P | 417718-11-7P | |
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| | 417718-19-5P | 417718-21-9P | 417718-23-1P | 417718-25-3P | |
| | 417718-26-4P | 417718-28-6P | 417718-30-0P | 417718-31-1P | 417718-32-2P |
| | 417718-34-4P | 417718-35-5P | 417718-36-6P | 417718-37-7P | 417718-39-9P |
| | 417718-40-2P | 417718-41-3P | 417718-42-4P | 417718-43-5P | 417718-44-6P |
| | 417718-45-7P | 417718-46-8P | 417718-47-9P | 417718-48-0P | 417718-49-1P |
| | 417718-50-4P | 417718-51-5P | 417718-52-6P | 417718-53-7P | 417718-54-8P |
| | 417718-55-9P | 417718-56-0P | 417718-57-1P | | |

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

| | | | | | | |
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| IT | 399-95-1P | 3898-47-3P | 4792-60-3P | 5264-02-8P | 6980-08-1P | 7251-09-4P |
| | 14549-38-3P | 17424-90-7P | 17576-39-5P | 17614-10-7P | 18031-97-5P | |
| | 39142-40-0P | 65141-00-6P | 65141-04-0P | 74889-21-7P | 81479-55-2P | |
| | 96783-89-0P | 97480-55-2P | 105130-28-7P | 124041-03-8P | 130035-46-0P | |
| | 185220-68-2P | 190060-72-1P | 221040-07-9P | 286371-87-7P | 347151-53-5P | |
| | 417720-95-7P | 417720-96-8P | 417720-97-9P | 417720-98-0P | 417720-99-1P | |
| | 417721-00-7P | 417721-01-8P | 417721-02-9P | 417721-03-0P | 417721-04-1P | |
| | 417721-05-2P | 417721-06-3P | 417721-07-4P | 417721-08-5P | 417721-09-6P | |
| | 417721-10-9P | 417721-11-0P | 417721-12-1P | 417721-13-2P | 417721-14-3P | |
| | 417721-15-4P | 417721-16-5P | 417721-17-6P | 417721-18-7P | 417721-19-8P | |
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| | 417721-25-6P | 417721-26-7P | 417721-27-8P | 417721-28-9P | 417721-29-0P | |
| | 417721-30-3P | 417721-31-4P | 417721-32-5P | 417721-33-6P | 417721-34-7P | |
| | 417721-35-8P | 417721-36-9P | 417721-37-0P | 417721-38-1P | 417721-39-2P | |
| | 417721-40-5P | 417721-41-6P | 417721-42-7P | 417721-43-8P | 417721-44-9P | |
| | 417721-45-0P | 417721-46-1P | 417721-47-2P | 417721-48-3P | 417721-49-4P | |
| | 417721-50-7P | 417721-51-8P | 417721-52-9P | 417721-53-0P | 417721-54-1P | |
| | 417721-55-2P | 417721-56-3P | 417721-57-4P | 417721-58-5P | 417721-59-6P | |
| | 417721-60-9P | 417721-61-0P | 417721-62-1P | 417721-63-2P | 417721-64-3P | |
| | 417721-65-4P | 417721-66-5P | 417721-67-6P | 417721-68-7P | 417721-69-8P | |
| | 417721-70-1P | 417721-71-2P | 417721-72-3P | 417721-73-4P | 417721-74-5P | |
| | 417721-75-6P | 417721-76-7P | 417721-77-8P | 417721-78-9P | | |
| | 417721-79-0P | 417721-80-3P | 417721-81-4P | 417721-82-5P | | |
| | 417721-83-6P | 417721-84-7P | 417721-85-8P | 417721-86-9P | 417721-87-0P | |
| | 417721-88-1P | 417721-89-2P | 417721-90-5P | 417721-91-6P | 417721-92-7P | |
| | 417721-93-8P | 417721-94-9P | 417721-95-0P | 417721-96-1P | | |
| | 417721-97-2P | 417721-98-3P | 417721-99-4P | 417722-00-0P | 417722-01-1P | |
| | 417722-02-2P | 417722-03-3P | 417722-04-4P | 417722-05-5P | | |
| | 417722-06-6P | 417722-07-7P | 417722-08-8P | 417722-10-2P | 417722-11-3P | |
| | 417722-12-4P | 417722-13-5P | 417722-14-6P | 417722-15-7P | 417722-16-8P | |
| | 417722-17-9P | 417722-18-0P | 417722-19-1P | 417722-20-4P | 417722-21-5P | |
| | 417722-22-6P | 417722-23-7P | 417722-24-8P | 417722-25-9P | 417722-26-0P | |
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| | 417722-32-8P | 417722-33-9P | 417722-34-0P | 417722-35-1P | 417722-36-2P | |
| | 417722-37-3P | 417722-38-4P | 417722-39-5P | 417722-40-8P | 417722-41-9P | |
| | 417722-42-0P | 417722-43-1P | 417722-44-2P | 417722-45-3P | 417722-46-4P | |
| | 417722-47-5P | 417722-48-6P | 417722-49-7P | 417722-50-0P | 417722-51-1P | |
| | 417722-52-2P | 417722-53-3P | 417722-54-4P | 417722-55-5P | 417722-56-6P | |
| | 417722-57-7P | 417722-58-8P | 417722-59-9P | 417722-60-2P | 417722-61-3P | |
| | 417722-62-4P | 417722-63-5P | 417722-64-6P | 417722-65-7P | 417722-66-8P | |
| | 417722-67-9P | 417722-69-1P | 417722-71-5P | 417722-73-7P | 417722-75-9P | |
| | 417722-76-0P | 417722-77-1P | 417722-78-2P | 417722-79-3P | 417722-81-7P | |
| | 417722-82-8P | 417722-83-9P | 417722-85-1P | 417722-87-3P | 417722-89-5P | |
| | 417722-91-9P | 417722-93-1P | 417722-95-3P | 417722-97-5P | 417722-99-7P | |
| | 417723-01-4P | 417723-03-6P | 417723-05-8P | 417723-07-0P | 417723-09-2P | |
| | 417723-11-6P | 417723-13-8P | 417723-15-0P | 417723-17-2P | 417723-19-4P | |
| | 417723-21-8P | 417723-23-0P | 417723-25-2P | 417723-27-4P | 417723-29-6P | |
| | 417723-31-0P | 417723-33-2P | 417723-35-4P | 417723-37-6P | | |

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

| | | | | | |
|----|--------------|--------------|--------------|--------------|--------------|
| IT | 417723-39-8P | 417723-41-2P | 417723-43-4P | 417723-44-5P | 417723-45-6P |
| | 417723-49-0P | 417723-51-4P | 417723-53-6P | 417723-54-7P | |
| | 417723-55-8P | 417723-56-9P | 417723-57-0P | 417723-58-1P | 417723-59-2P |
| | 417723-60-5P | 417723-61-6P | 417723-62-7P | 417723-63-8P | 417723-64-9P |
| | 417723-65-0P | 417723-66-1P | 417723-67-2P | 417723-68-3P | 417723-70-7P |
| | 417723-71-8P | 417723-72-9P | 417723-73-0P | 417723-74-1P | 417723-75-2P |
| | 417723-76-3P | 417723-77-4P | 417723-78-5P | 417723-80-9P | 417723-81-0P |

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| | | | | |
|--------------|--------------|--------------|--------------|--------------|
| 417723-82-1P | 417723-83-2P | 417723-84-3P | 417723-85-4P | 417723-87-6P |
| 417723-89-8P | 417723-91-2P | 417723-93-4P | 417723-94-5P | 417723-95-6P |
| 417723-96-7P | 417723-97-8P | 417723-98-9P | 417723-99-0P | 417724-00-6P |
| 417724-01-7P | 417724-02-8P | 417724-03-9P | 417724-04-0P | 417724-05-1P |
| 417724-06-2P | 417724-07-3P | 417724-08-4P | 417724-09-5P | 417724-10-8P |
| 417724-11-9P | 417724-12-0P | 417724-13-1P | 417724-14-2P | 417724-15-3P |
| 417724-16-4P | 417724-17-5P | 417724-18-6P | 417724-19-7P | 417724-20-0P |
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| 417724-28-8P | 417724-29-9P | 417724-30-2P | 417724-31-3P | 417724-32-4P |
| 417724-33-5P | 417724-34-6P | 417724-35-7P | 417724-36-8P | 417724-37-9P |
| 417724-38-0P | 417724-39-1P | 417724-40-4P | 417724-41-5P | 417724-42-6P |
| 417724-43-7P | 417724-44-8P | 417724-45-9P | 417724-46-0P | 417724-47-1P |
| 417724-48-2P | 417724-49-3P | 417724-50-6P | 417724-51-7P | 417724-52-8P |
| 417724-53-9P | 417724-54-0P | 417724-55-1P | 417724-56-2P | 417724-57-3P |
| 417724-58-4P | 417724-59-5P | 417724-60-8P | 417724-61-9P | 417724-62-0P |
| 417724-63-1P | 417724-64-2P | 417724-65-3P | 417724-66-4P | 417724-67-5P |
| 417724-68-6P | 417724-69-7P | 417724-70-0P | 417724-71-1P | 417724-72-2P |
| 417724-74-4P | 417724-75-5P | 417724-80-2P | 417724-81-3P | 417724-86-8P |
| 417724-87-9P | 417724-88-0P | 417724-89-1P | 417724-90-4P | 417724-91-5P |
| 417724-92-6P | 417724-94-8P | 417724-95-9P | 417724-96-0P | 417724-98-2P |
| 417724-99-3P | 417725-00-9P | 417725-01-0P | 417725-02-1P | 417725-05-4P |
| 417725-08-7P | 417725-09-8P | | | |

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

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REFERENCE COUNT: 117 THERE ARE 117 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 2 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:691680 HCAPLUS Full-text

DOCUMENT NUMBER: 147:118041

TITLE: Omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors

INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: U.S., 52pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| US 7235576 | B1 | 20070626 | US 2002-42203 | 20020111 <-- |
| US 20030144278 | A1 | 20030731 | US 2002-283248 | 20021030 <-- |
| US 20080108672 | A1 | 20080508 | US 2007-768104 | 20070625 <-- |
| PRIORITY APPLN. INFO.: | | | US 2001-367380P | P 20010112 <-- |
| | | | US 2002-42203 | A1 20020111 <-- |

OTHER SOURCE(S): MARPAT 147:118041

AB Aryl ureas A-NHCONH-B [A, B = C5-40 (poly)aryl, optionally containing 0-4 N, O, S heteroatoms, optionally substituted by (hetero)aryl, (hetero)aryloxy, halo, cyano, nitro, alkoxy, alkylthio, amino, hydroxyalkyl, sulfo, acyl, carboxamido-groups], useful as Raf-kinase inhibitors for treatment and

inhibition of cancerous cell growth, were prepared by standard synthetic procedures by reactions of the corresponding isocyanates with aromatic amines and tested for inhibition of Raf kinase and growth of human tumor cell lines HCT116 and DLD-1, exhibiting IC50 values of 1 nM to 10 μ M. In an example, N-(4-chloro-3-trifluoromethylphenyl)-N'-[4-(2-methylaminocarbonyl-4-pyridinyloxy)phenyl]urea was prepared by reaction of 65.9 mmol of 4-chloro-3-trifluoromethylphenyl isocyanate with 65.77 mmol of 4-(2-methylaminocarbonyl-4-pyridinyloxy)aniline in CH2Cl2 at room temperature for 22 h with 93% yield.

IT 943024-26-8P

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors

for treatment and inhibition of cancerous cell growth)

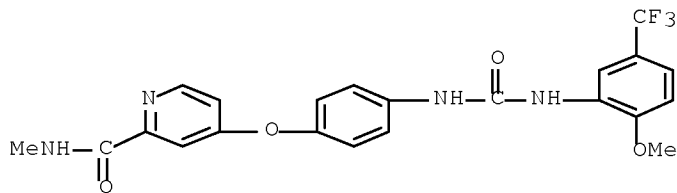
RN 943024-26-8 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl-, 4-methylbenzenesulfonate (1:1) (CA INDEX NAME)

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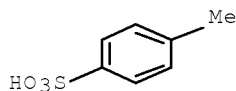
CMF C22 H19 F3 N4 O4



CM 2

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CMF C7 H8 O3 S



INCL 514388000; 514354000; 514358000; 514597000; 514552000; 546329000; 546339000; 564054000; 564055000; 564336000

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 63

IT 943024-26-8P

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL

10/590724

(Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors

for treatment and inhibition of cancerous cell growth)

IT 475207-59-1P 943024-27-9P 943024-28-0P
943024-29-1P

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors

for treatment and inhibition of cancerous cell growth)

IT 284461-44-5P 284461-89-8P 284462-67-5P 284462-68-6P
284462-69-7P 284462-71-1P

RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors

for treatment and inhibition of cancerous cell growth)

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RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors

for treatment and inhibition of cancerous cell growth)

IT 98-98-6, 2-Pyridinecarboxylic acid 99-93-4 99-98-9,
1,4-Benzenediamine, N,N-dimethyl- 109-85-3 110-13-4, Acetonylacetone
123-30-8, 4-Aminophenol 320-51-4 327-78-6 349-65-5 350-46-9
371-40-4 393-36-2 462-08-8, 3-Pyridinamine 591-27-5, 3-Aminophenol
610-35-5 619-08-9 626-61-9, 4-Chloropyridine 883-99-8 1121-78-4
1193-02-8 1215-98-1 1664-40-0, 1,2-Ethanediamine, N-phenyl-
1877-71-0, 1,3-Benzenedicarboxylic acid, monomethyl ester 2038-03-1,

10/590724

4-Morpholineethanamine 2252-63-3 2524-67-6 2835-95-2 2835-99-6
2905-24-0 3535-88-4 3964-52-1 4548-45-2 4795-29-3,
2-Tetrahydrofuranmethanamine 6310-19-6 6628-77-9 6927-86-2
16588-75-3 26171-06-2 27578-60-5, 1-Piperidineethanamine 29264-35-5
30766-22-4 30806-83-8 34803-66-2 36265-31-3 51639-48-6
150009-83-9 284462-06-2 284462-72-2 284462-73-3
284462-76-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of carboxyaryl-substituted diarylureas as Raf kinase
inhibitors

for treatment and inhibition of cancerous cell growth)

REFERENCE COUNT: 223 THERE ARE 223 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L110 ANSWER 3 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1314363 HCAPLUS Full-text

DOCUMENT NUMBER: 144:57544

TITLE: Antibody drug conjugates and uses for cancer therapy

INVENTOR(S): Ebens, Allen J., Jr.; Jacobson, Frederic S.; Polakis,
Paul; Schwall, Ralph H.; Sliwowski, Mark X.; Spencer,
Susan D.

PATENT ASSIGNEE(S): Genentech, Inc., USA

SOURCE: PCT Int. Appl., 110 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 160

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|--------------|
| WO 2005117986 | A2 | 20051215 | WO 2005-US18829 | 20050531 |
| WO 2005117986 | A3 | 20060615 | | |
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| AT 310810 | T | 20051215 | AT 2001-127791 | 19980916 <-- |
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| NZ 528704 | A | 20050225 | NZ 1999-528704 | 19990308 <-- |
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| NZ 523208 | A | 20041224 | NZ 2000-523208 | 20000211 <-- |
| NZ 523209 | A | 20041224 | NZ 2000-523209 | 20000211 <-- |
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| CA 2481691 | A1 | 20010308 | CA 2000-2481691 | 20000824 <-- |
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10/590724

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| JP 2004520810 | T | 20040715 | JP 2002-522275 | 20010823 <-- |
| US 20030073129 | A1 | 20030417 | US 2001-946374 | 20010904 <-- |
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| EP 1397383 | A2 | 20040317 | EP 2001-990229 | 20011213 <-- |
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| CA 2449602 | A1 | 20021219 | CA 2002-2449602 | 20020403 <-- |
| WO 2002101069 | A2 | 20021219 | WO 2002-US10513 | 20020403 <-- |
| WO 2002101069 | A3 | 20030904 | | |
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| AU 2002303231 | A1 | 20021223 | AU 2002-303231 | 20020403 <-- |
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| US 20030207351 | A1 | 20031106 | US 2002-140473 | 20020506 <-- |
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10/590724

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10/590724

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| AU 2003204357 | A1 | 20030619 | AU 2003-204357 | 20030526 <-- |
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| AU 2003257515 | A1 | 20031120 | AU 2003-257515 | 20031023 <-- |
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| AU 2003259607 | A1 | 20031127 | AU 2003-259607 | 20031031 <-- |
| AU 2003259607 | B2 | 20051103 | | |
| US 20040258710 | A1 | 20041223 | US 2004-791618 | 20040302 <-- |
| US 20050019823 | A1 | 20050127 | US 2004-931886 | 20040831 <-- |
| US 20050187382 | A1 | 20050825 | US 2004-950374 | 20040923 <-- |
| US 20050153396 | A1 | 20050714 | US 2004-955952 | 20040929 <-- |
| US 20050153348 | A1 | 20050714 | US 2004-20604 | 20041221 <-- |
| US 20050176041 | A1 | 20050811 | US 2004-26279 | 20041230 <-- |
| US 20050214819 | A1 | 20050929 | US 2005-30464 | 20050105 <-- |
| US 20050164266 | A1 | 20050728 | US 2005-36582 | 20050113 <-- |
| US 20050170396 | A1 | 20050804 | US 2005-36869 | 20050114 <-- |
| US 20050202475 | A1 | 20050915 | US 2005-38328 | 20050118 <-- |
| US 20050176046 | A1 | 20050811 | US 2005-46650 | 20050128 <-- |
| US 20050176104 | A1 | 20050811 | US 2005-52503 | 20050204 <-- |
| US 20050136515 | A1 | 20050623 | US 2005-56802 | 20050211 <-- |
| US 20050136475 | A1 | 20050623 | US 2005-60652 | 20050216 <-- |
| US 20050158830 | A1 | 20050721 | US 2005-80062 | 20050314 |
| US 20050214846 | A1 | 20050929 | US 2005-117757 | 20050427 <-- |
| AU 2005249490 | A1 | 20051215 | AU 2005-249490 | 20050531 |
| CA 2567520 | A1 | 20051215 | CA 2005-2567520 | 20050531 |
| EP 1753463 | A2 | 20070221 | EP 2005-804852 | 20050531 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |
| CN 1993146 | A | 20070704 | CN 2005-80026066 | 20050531 |
| BR 2005010883 | A | 20071226 | BR 2005-10883 | 20050531 |
| JP 2008501029 | T | 20080117 | JP 2007-515417 | 20050531 |
| AU 2005205752 | A1 | 20050922 | AU 2005-205752 | 20050831 <-- |
| AU 2005205752 | B2 | 20070607 | | |
| AU 2005205754 | A1 | 20050922 | AU 2005-205754 | 20050831 <-- |
| AU 2005205754 | B2 | 20070920 | | |
| AU 2005205755 | A1 | 20050922 | AU 2005-205755 | 20050831 <-- |
| AU 2005205755 | B2 | 20071004 | | |

10/590724

| | | | | | |
|------------------------|----|----------|-----------------|----------|--------------|
| AU 2005205758 | A1 | 20050922 | AU 2005-205758 | 20050831 | <-- |
| AU 2005205758 | B2 | 20070913 | | | |
| US 20070191270 | A1 | 20070816 | US 2005-234694 | 20050922 | <-- |
| US 20080166294 | A1 | 20080710 | US 2006-461752 | 20060801 | <-- |
| JP 2007037551 | A | 20070215 | JP 2006-221327 | 20060814 | <-- |
| IN 2006DN07052 | A | 20070713 | IN 2006-DN7052 | 20061123 | |
| US 20070269446 | A1 | 20071122 | US 2006-564171 | 20061128 | <-- |
| MX 2006PA14065 | A | 20070131 | MX 2006-PA14065 | 20061130 | |
| KR 2007037575 | A | 20070405 | KR 2006-725240 | 20061130 | |
| AU 2006252290 | A1 | 20070125 | AU 2006-252290 | 20061229 | <-- |
| NO 2006006075 | A | 20070228 | NO 2006-6075 | 20061229 | |
| US 20070219350 | A1 | 20070920 | US 2007-801111 | 20070507 | |
| AU 2007203155 | A1 | 20070726 | AU 2007-203155 | 20070705 | <-- |
| AU 2007203291 | A1 | 20070802 | AU 2007-203291 | 20070717 | <-- |
| AU 2007214325 | A1 | 20070920 | AU 2007-214325 | 20070830 | <-- |
| AU 2008201807 | A1 | 20080515 | AU 2008-201807 | 20080424 | |
| AU 2008201995 | A1 | 20080529 | AU 2008-201995 | 20080506 | <-- |
| AU 2008201996 | A1 | 20080529 | AU 2008-201996 | 20080506 | <-- |
| AU 2008201998 | A1 | 20080529 | AU 2008-201998 | 20080506 | <-- |
| AU 2008202000 | A1 | 20080529 | AU 2008-202000 | 20080506 | <-- |
| AU 2008202004 | A1 | 20080529 | AU 2008-202004 | 20080506 | <-- |
| AU 2008202007 | A1 | 20080529 | AU 2008-202007 | 20080506 | <-- |
| PRIORITY APPLN. INFO.: | | | US 2004-576517P | P | 20040601 |
| | | | US 2004-616098P | P | 20041005 |
| | | | US 1997-63128P | P | 19971024 <-- |
| | | | US 1998-83742P | P | 19980430 <-- |
| | | | US 1998-84366P | P | 19980505 <-- |
| | | | US 1998-85339P | A1 | 19980513 <-- |
| | | | US 1998-87106P | P | 19980528 <-- |
| | | | US 1998-88326P | P | 19980604 <-- |
| | | | US 1998-88217P | P | 19980605 <-- |
| | | | US 1998-88655P | P | 19980609 <-- |
| | | | US 1998-89947P | P | 19980619 <-- |
| | | | US 1998-90676P | P | 19980625 <-- |
| | | | US 1998-91982P | P | 19980707 <-- |
| | | | AU 1998-84850 | A3 | 19980714 <-- |
| | | | US 1998-94651P | A1 | 19980730 <-- |
| | | | US 1998-96012P | P | 19980810 <-- |
| | | | US 1998-97022P | P | 19980818 <-- |
| | | | US 1998-97954P | P | 19980826 <-- |
| | | | US 1998-97974P | P | 19980826 <-- |
| | | | US 1998-97979P | P | 19980826 <-- |
| | | | AU 1998-93881 | A3 | 19980914 <-- |
| | | | AU 1998-93178 | A3 | 19981002 <-- |
| | | | AU 1999-10703 | A3 | 19981007 <-- |
| | | | US 1998-105169P | P | 19981022 <-- |
| | | | US 1998-63561P | P | 19981028 <-- |
| | | | AU 1999-11260 | A3 | 19981029 <-- |
| | | | AU 1999-12883 | A3 | 19981029 <-- |
| | | | WO 1998-US22992 | W | 19981029 <-- |
| | | | AU 1999-30721 | A3 | 19990308 <-- |
| | | | US 1999-131293P | P | 19990427 <-- |
| | | | US 1999-133459P | P | 19990511 <-- |
| | | | US 1999-140650P | P | 19990622 <-- |
| | | | US 1999-149395P | P | 19990817 <-- |
| | | | US 1999-151689P | P | 19990831 <-- |
| | | | AU 1999-55908 | A3 | 19990901 <-- |
| | | | CA 1999-2344465 | A3 | 19991005 <-- |
| | | | AU 2000-17482 | A3 | 19991130 <-- |
| | | | AU 2000-17499 | A3 | 19991202 <-- |

10/590724

| | |
|-----------------|-----------------|
| EP 1999-960644 | A3 19991202 <-- |
| AU 2000-28794 | A3 20000211 <-- |
| US 2000-189320P | P 20000314 <-- |
| US 2000-189328P | P 20000314 <-- |
| US 2000-190828P | P 20000321 <-- |
| US 2000-191048P | P 20000321 <-- |
| US 2000-191314P | P 20000321 <-- |
| US 2000-193032P | P 20000329 <-- |
| US 2000-193053P | P 20000329 <-- |
| US 2000-194449P | P 20000404 <-- |
| US 2000-194647P | P 20000404 <-- |
| US 2000-195975P | P 20000411 <-- |
| US 2000-196000P | P 20000411 <-- |
| US 2000-196187P | P 20000411 <-- |
| US 2000-196820P | XX 20000411 <-- |
| US 2000-198121P | P 20000418 <-- |
| US 2000-198585P | P 20000418 <-- |
| US 2000-199397P | P 20000425 <-- |
| US 2000-199550P | P 20000425 <-- |
| US 2000-201516P | P 20000503 <-- |
| US 2000-204675P | P 20000517 <-- |
| US 2000-227133P | P 20000822 <-- |
| CA 2000-2380355 | A3 20000824 <-- |
| US 2000-232887P | P 20000915 <-- |
| US 2000-690189 | A3 20001016 <-- |
| JP 2002-576286 | A3 20010322 <-- |
| US 2001-816920 | B1 20010322 <-- |
| EP 2001-939834 | A3 20010601 <-- |
| EP 2004-5726 | A3 20010601 <-- |
| US 2001-880457 | A 20010612 <-- |
| US 2001-882636 | B1 20010614 <-- |
| AU 2001-271938 | A3 20010710 <-- |
| AU 2001-71938 | T0 20010710 <-- |
| US 2001-927796 | B1 20010809 <-- |
| WO 2001-US26626 | W 20010823 <-- |
| US 2001-990711 | A1 20011114 <-- |
| US 2001-992521 | B1 20011114 <-- |
| WO 2001-US48938 | W 20011213 <-- |
| US 2002-52586 | A1 20020115 <-- |
| WO 2002-US10513 | W 20020403 <-- |
| US 2002-123155 | A1 20020415 <-- |
| US 2002-127825 | A1 20020422 <-- |
| US 2002-127966 | B1 20020423 <-- |
| US 2002-141703 | A1 20020508 <-- |
| US 2002-145627 | A1 20020514 <-- |
| US 2002-145751 | A 20020514 <-- |
| US 2002-146793 | A1 20020515 <-- |
| US 2002-197703 | B1 20020717 <-- |
| US 2002-197708 | A1 20020717 <-- |
| US 2002-197942 | B1 20020718 <-- |
| US 2002-199666 | A1 20020718 <-- |
| US 2002-199464 | B1 20020719 <-- |
| US 2002-211858 | A1 20020802 <-- |
| AU 2002-330015 | A3 20020911 <-- |
| AU 2002-367318 | A3 20021230 <-- |
| AU 2003-200137 | A3 20030115 <-- |
| AU 2003-203679 | A3 20030411 <-- |
| AU 2003-261484 | A 20031106 <-- |
| US 2003-520842P | P 20031117 <-- |
| US 2003-532426P | P 20031224 <-- |

10/590724

| | |
|-----------------|-------------|
| US 2004-797366 | A1 20040309 |
| US 2004-872972 | A1 20040621 |
| US 2004-989826 | A2 20041116 |
| WO 2004-US38262 | A2 20041116 |
| AU 2005-200179 | A3 20050114 |
| US 2005-141344 | A2 20050531 |
| WO 2005-US18829 | W 20050531 |
| US 2006-461752 | A2 20060801 |

OTHER SOURCE(S): MARPAT 144:57544

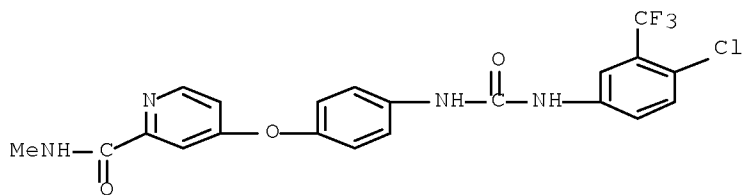
AB The present invention relates to antibody-drug conjugate compds. with a formula of Ab-(L-D)_p where 1 to 8 (p) maytansinoid drug moieties (D) are covalently linked by L to an antibody (Ab) which binds to an ErbB receptor, or which binds to one or more tumor-associated antigens or cell-surface receptors. These compds. may be used in methods of diagnosis or treatment of cancer, and other diseases and disorders.

IT 284461-73-0, Sorafenib

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody drug conjugates and uses for cancer therapy)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c
arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K047-48

ICS A61P035-00; G01N033-574

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 15

IT 51-21-8, 5-FU 58-05-9, Leucovorin 4856-87-5 5132-30-9 28537-70-4,
1,4-Bis-maleimidobutane 53123-88-9, Rapamycin 61825-94-3, Oxaliplatin
64987-85-5, SMCC 71865-37-7 86099-06-1 112809-51-5, Letrozole
115597-84-7 129453-61-8, Fulvestrant 179324-69-7, Bortezomib
180288-69-1, Trastuzumab 183321-74-6, Erlotinib 184475-35-2, Gefitinib
189013-00-1 193275-84-2, Lonaferinib 212142-18-2, ZK222584
216974-75-3, Bevacizumab 220127-57-1, Imatinib mesylate 231277-92-2,
Lapatinib 284461-73-0, Sorafenib 557795-19-4, Sutent

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antibody drug conjugates and uses for cancer therapy)

L110 ANSWER 4 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:470256 HCAPLUS Full-text

DOCUMENT NUMBER: 143:20052

TITLE: Urea derivatives as kinase modulators

INVENTOR(S): Milanov, Zdravko V.; Patel, Hitesh K.; Grotzfeld,
Robert M.; Mehta, Shamal A.; Andiliy, Lai G.;
Lockhart, David J.

PATENT ASSIGNEE(S): Ambit Biosciences Corporation, USA

10/590724

SOURCE: PCT Int. Appl., 350 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|----------------|
| WO 2005048948 | A2 | 20050602 | WO 2004-US38288 | 20041115 <-- |
| WO 2005048948 | A3 | 20050728 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2004291147 | A1 | 20050602 | AU 2004-291147 | 20041115 <-- |
| CA 2545711 | A1 | 20050602 | CA 2004-2545711 | 20041115 <-- |
| US 20050148605 | A1 | 20050707 | US 2004-989745 | 20041115 <-- |
| US 20050165031 | A1 | 20050728 | US 2004-989814 | 20041115 <-- |
| US 20050165024 | A1 | 20050728 | US 2004-989824 | 20041115 <-- |
| US 20050165074 | A1 | 20050728 | US 2004-990007 | 20041115 <-- |
| US 20050171171 | A1 | 20050804 | US 2004-989766 | 20041115 <-- |
| US 20050171172 | A1 | 20050804 | US 2004-989823 | 20041115 <-- |
| US 20050192314 | A1 | 20050901 | US 2004-990195 | 20041115 <-- |
| US 20050197371 | A1 | 20050908 | US 2004-990194 | 20041115 <-- |
| US 20050261315 | A1 | 20051124 | US 2004-989623 | 20041115 <-- |
| US 20050267182 | A1 | 20051201 | US 2004-989717 | 20041115 <-- |
| EP 1684762 | A2 | 20060802 | EP 2004-811122 | 20041115 <-- |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS | | | |
| JP 2007512255 | T | 20070517 | JP 2006-539991 | 20041115 <-- |
| PRIORITY APPLN. INFO.: | | | US 2003-520273P | P 20031113 <-- |
| | | | US 2003-527094P | P 20031203 <-- |
| | | | US 2003-531082P | P 20031218 <-- |
| | | | US 2003-531243P | P 20031218 <-- |
| | | | WO 2004-US38288 | W 20041115 |

OTHER SOURCE(S): MARPAT 143:20052

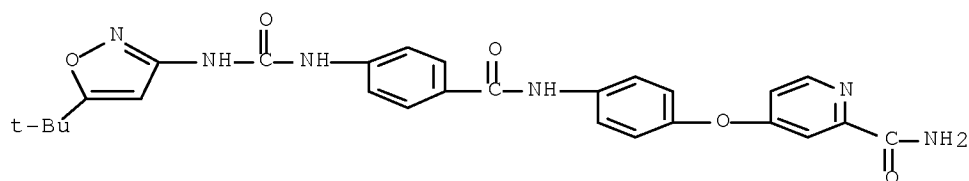
AB The invention provides methods and compns. for treating conditions mediated by various kinases wherein derivs. of urea compds. are employed. The invention also provides methods of using the compds. and/or compns. in the treatment of a variety of diseases and unwanted conditions in subjects such as cellular proliferative disorders.

IT 852669-21-7

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (urea derivs. as kinase modulators for treatment of cellular proliferative disorders)

RN 852669-21-7 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[4-[[[5-(1,1-dimethylethyl)-3-isoxazolyl]amino]carbonyl]amino]benzoyl]amino]phenoxy]- (CA INDEX NAME)



IC ICM A61K

CC 1-12 (Pharmacology)

Section cross-reference(s): 7, 28

| | | | | | |
|----|-------------|-------------|-------------|-------------|-------------|
| IT | 55807-76-6 | 70584-44-0 | 219793-76-7 | 223724-76-3 | 228998-90-1 |
| | 228999-65-3 | 228999-75-5 | 228999-78-8 | 229000-17-3 | 229000-21-9 |
| | 229000-24-2 | 229000-37-7 | 229000-38-8 | 229000-39-9 | 229000-40-2 |
| | 229000-42-4 | 229000-43-5 | 229000-62-8 | 229154-75-0 | 229155-18-4 |
| | 249762-62-7 | 256471-16-6 | 256471-19-9 | 256471-27-9 | 263385-47-3 |
| | 263385-48-4 | 294657-41-3 | 301689-36-1 | 389070-24-0 | 432042-02-9 |
| | 433327-37-8 | 648408-76-8 | 649663-80-9 | 680215-51-4 | 691850-16-5 |
| | 691850-18-7 | 693218-67-6 | 693218-69-8 | 696585-93-0 | 705286-70-0 |
| | 705286-71-1 | 705286-72-2 | 705286-73-3 | 706776-96-7 | 852668-45-2 |
| | 852668-46-3 | 852668-47-4 | 852668-48-5 | 852668-49-6 | 852668-50-9 |
| | 852668-51-0 | 852668-52-1 | 852668-53-2 | 852668-54-3 | 852668-55-4 |
| | 852668-56-5 | 852668-58-7 | 852668-59-8 | 852668-60-1 | 852668-61-2 |
| | 852668-62-3 | 852668-63-4 | 852668-64-5 | 852668-65-6 | 852668-66-7 |
| | 852668-67-8 | 852668-68-9 | 852668-69-0 | 852668-70-3 | 852668-71-4 |
| | 852668-72-5 | 852668-73-6 | 852668-74-7 | 852668-75-8 | 852668-76-9 |
| | 852668-77-0 | 852668-78-1 | 852668-79-2 | 852668-80-5 | 852668-81-6 |
| | 852668-82-7 | 852668-83-8 | 852668-84-9 | 852668-85-0 | 852668-86-1 |
| | 852668-87-2 | 852668-88-3 | 852668-89-4 | 852668-90-7 | 852668-91-8 |
| | 852668-92-9 | 852668-93-0 | 852668-94-1 | 852668-95-2 | 852668-96-3 |
| | 852668-97-4 | 852668-98-5 | 852668-99-6 | 852669-00-2 | 852669-01-3 |
| | 852669-02-4 | 852669-03-5 | 852669-04-6 | 852669-05-7 | 852669-06-8 |
| | 852669-07-9 | 852669-08-0 | 852669-09-1 | 852669-10-4 | 852669-11-5 |
| | 852669-12-6 | 852669-13-7 | 852669-14-8 | 852669-15-9 | 852669-16-0 |
| | 852669-17-1 | 852669-18-2 | 852669-19-3 | 852669-20-6 | 852669-21-7 |
| | 852669-22-8 | 852669-24-0 | 852669-25-1 | 852669-26-2 | 852669-27-3 |
| | 852669-28-4 | 852669-29-5 | 852669-30-8 | 852669-31-9 | 852669-32-0 |
| | 852669-33-1 | 852669-34-2 | 852669-35-3 | 852669-36-4 | 852669-37-5 |
| | 852669-38-6 | 852669-39-7 | 852669-40-0 | 852669-41-1 | 852669-42-2 |
| | 852669-43-3 | 852669-44-4 | 852669-45-5 | 852669-46-6 | 852669-47-7 |
| | 852669-48-8 | 852669-49-9 | 852669-50-2 | 852669-51-3 | 852669-52-4 |
| | 852669-53-5 | 852669-54-6 | 852669-55-7 | 852669-56-8 | 852669-57-9 |
| | 852669-58-0 | 852669-59-1 | 852669-60-4 | 852669-61-5 | 852669-62-6 |
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| | 852669-90-0 | 852669-92-2 | 852669-95-5 | 852670-00-9 | 852670-01-0 |
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| | 852670-07-6 | 852670-08-7 | 852670-09-8 | 852670-10-1 | 852670-11-2 |
| | 852670-12-3 | 852670-13-4 | 852670-14-5 | 852670-15-6 | 852670-16-7 |
| | 852670-17-8 | 852670-18-9 | 852670-19-0 | 852670-20-3 | 852670-21-4 |
| | 852670-22-5 | 852670-23-6 | 852670-24-7 | 852670-25-8 | 852670-26-9 |
| | 852670-27-0 | 852670-28-1 | 852670-29-2 | 852670-30-5 | 852670-31-6 |
| | 852670-32-7 | 852670-33-8 | 852670-34-9 | 852670-35-0 | 852670-38-3 |
| | 852670-39-4 | 852670-40-7 | 852670-41-8 | 852670-42-9 | 852670-43-0 |

10/590724

852670-44-1 852670-45-2 852670-46-3 852670-47-4 852670-48-5
852670-49-6

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(urea derivs. as kinase modulators for treatment of cellular
proliferative disorders)

L110 ANSWER 5 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:470251 HCAPLUS Full-text
DOCUMENT NUMBER: 143:19957
TITLE: Combination therapy comprising a cyclooxygenase 2
(COX-2) inhibitor and an antineoplastic agent for
treatment or prevention of neoplasia
INVENTOR(S): Masferrer, Jaime L.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 317 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|--------------|
| WO 2005048942 | A2 | 20050602 | WO 2004-US38019 | 20041115 <-- |
| WO 2005048942 | A3 | 20060330 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

| | | | | |
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| US 20050227929 | A1 | 20051013 | US 2004-989192 | 20041115 <-- |
| PRIORITY APPLN. INFO.: | | | US 2003-519701P | P 20031113 <-- |

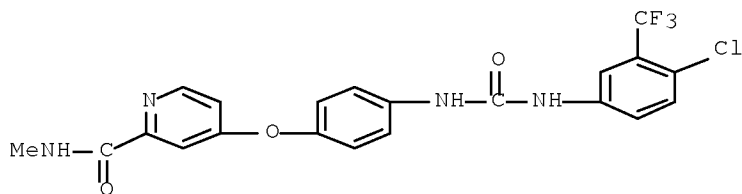
AB A method for treating or preventing neoplasia or a neoplasia-related disorder
in a subject is provided, the method comprising administering to the subject
an effective amount of a combination comprising a COX-2 inhibitor and an
antineoplastic agent.

IT 284461-73-0, BAY 439006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(cyclooxygenase 2 inhibitor-antineoplastic agent combination for
treatment or prevention of neoplasia)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c
arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K
 CC 1-6 (Pharmacology)
 IT 74-79-3D, L-Arginine, monomethyl derivs. 103-82-2D, Phenylacetic acid, derivs. 254-04-6D, Benzopyran, derivs. 355-25-9, NC 100100 646-08-2, β -Alethine 1400-61-9, Nystatin 1821-33-6 2353-33-5, 5-Aza-2'-deoxycytidine 5072-26-4, Buthionine sulfoximine 7689-03-4D, Camptothecin, glycoconjugate 9005-49-6, Dalteparin, biological studies 9014-42-0, RH-TPO 9074-87-7, Carboxypeptidase G2 18472-51-0, Oramed 19388-87-5, Taurolidine 33069-62-4, Paclitaxel 41941-56-4, Tocladesine 82855-09-2, Combretastatin 82952-64-5, Trimetrexate glucuronate 89778-26-7, GTx 006 97919-22-7 108560-70-9, Gallium maltolate 115427-51-5, INX-3280 118694-43-2, ILX 23-7553 128517-07-7 134774-45-1, Rasburicase 149882-10-0, Lurtotecan 152044-54-7, Epothilone B 152044-54-7D, Epothilone B, analogs 152459-95-5, Imatinib 156053-89-3, ADL 8-2698 160237-25-2, BMS-184476 162011-90-7, Rofecoxib 162635-04-3, CCI-779 169590-42-5, Celecoxib 170729-80-3, Aprepitant 172481-83-3, BMS 188797 173424-77-6, VNP-40101M 173937-91-2, Atrasentan 181695-72-7, Valdecocixib 186348-23-2, BAY 59-8862 188968-51-6, Cilengitide 191732-72-6, CDC 501 192391-48-3, Bexxar 192658-64-3 192819-27-5, CDC-801 195533-53-0, T-138067 195987-41-8 198470-84-7, Parecoxib 198470-85-8, Parecoxibsodium 198480-55-6, ERA 923 202409-33-4, Etoricocixib 205923-56-4, Cetuximab 209783-80-2, MS-275 209810-58-2, Aranesp 216503-58-1, BEC2 216974-75-3, Bevacizumab 219527-63-6, Repifermin 219989-84-1, BMS-247550 220578-59-6, Mylotarg 220991-20-8, Lumiracoxib 227619-96-7, CP-461 231277-92-2, GW-572016 236391-66-5, GTI 2040 236391-67-6, GTI 2501 246861-96-1, SB 251353 257933-82-7, EKB-569 259188-38-0, BMS-275291 261944-52-9 263351-82-2 267243-28-7 ~~284461-73-0~~, BAY 439006 288392-69-8, MEDI-507 289499-45-2, CI-1033 321309-50-6, NC-100150 340014-19-9, Melacine 380907-94-8, Cytotoxin SS1(dsFv)-PE38 (synthetic) 428438-54-4, SPD 424 439153-64-7, CP 609754 447471-67-2, MG-98 543726-73-4, IMC 1C11 623174-20-9, ILX 651 791096-83-8, SD 01 845680-07-1, Lapuleucel-T 848866-33-1, T 900607 852286-49-8 852834-17-4, PK 412 852834-62-9D, TNT 1B, I131 labeled 852834-90-3, KSB 309 852834-96-9, SB 310 852835-00-8, NBI 3001 852835-01-9, APC 8020 852835-30-4, RK 0202 852835-36-0, SR 29142 852835-43-9, Stemgen 852835-52-0, ALVAC B 7.1 852835-53-1, GnRH Pharmaccine 852836-15-8, rV-MUC 1 852836-20-5, CaPVax
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

L110 ANSWER 6 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2005:409543 HCAPLUS Full-text
 DOCUMENT NUMBER: 142:457053
 TITLE: Human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and

siRNA, and their use for enhancing apoptosis in cancer therapy
 INVENTOR(S): Lacasse, Eric; McManus, Daniel
 PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
 SOURCE: PCT Int. Appl., 112 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2005042558 | A1 | 20050512 | WO 2004-CA1902 | 20041029 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 20050148535 | A1 | 20050707 | US 2004-975974 | 20041028 <-- |
| CA 2542904 | A1 | 20050512 | CA 2004-2542904 | 20041029 <-- |
| EP 1682565 | A1 | 20060726 | EP 2004-789809 | 20041029 <-- |
| R: DE, FR, GB | | | | |
| JP 2007510408 | T | 20070426 | JP 2006-537024 | 20041029 <-- |
| PRIORITY APPLN. INFO.: | | | US 2003-516192P | P 20031030 <-- |
| | | | WO 2004-CA1902 | W 20041029 |

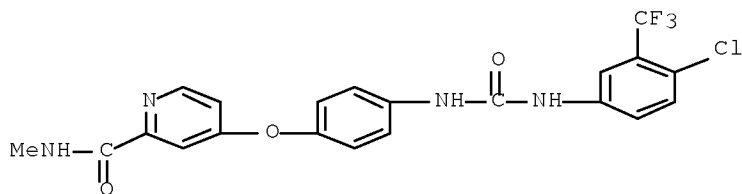
AB The invention provides nucleobase oligomers and oligonucleotide duplexes that inhibit expression of an IAP (inhibitor of apoptosis protein), and methods for using them to induce apoptosis in a cell. Specifically, the invention provides nucleic acid sequences for siRNAs and shRNAs that target human XIAP, HIAP-1 or HIAP-2 genes. The nucleobase oligomers and oligomer complexes of the present invention may also be used to form pharmaceutical compns. The invention also features methods for enhancing apoptosis in a cell by administering a nucleobase oligomer or oligomer complex of the invention in combination with a chemotherapeutic or chemosensitizing agent. RNAi sequences and vectors producing shRNA (short hairpin RNA) were transfected into HeLa cells and evaluated for their effect on XIAP, cIAP-1, or cIAP-2 protein levels. XIAP protein could also be reduced by RNAi clones in transfected breast cancer cell line MDA-MB-231. In addition, cell survival was reduced in XIAP RNAi transfected breast cancer cell line after the transfected cells were treated with TRAIL (tumor necrosis factor-related apoptosis inducing ligand).

IT 284461-73-0, BAY-43-9006

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c
 arboxyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07H021-00
ICS A61K048-00; A61K031-7088; A61K031-713; A61P035-00; C12N015-85

CC 1-6 (Pharmacology)
Section cross-reference(s): 3, 6, 13, 14

IT 195612-80-7, Galarubicin 196488-72-9, Ranpirnase 199796-52-6,
Taxoprexin 200484-11-3, CHS-828 201044-96-4, SB-T-1250 203258-60-0,
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D 24851 204318-14-9, Edotreotide 205923-56-4, C225 206873-63-4,
Tariquidar 207862-44-0, KW-2170 209783-80-2, MS-275 209973-83-1,
BLP-25 212007-18-6, Symplostatin 1 212141-54-3, Vatalanib
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246252-04-0, Lutetium texaphyrin 250693-48-2, G17DT 252916-29-3,
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Palladium bacteriopheophorbide a 284461-73-0, BAY-43-9006
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848871-07-8, CBT-1 848871-42-1, CDC-394 848872-94-6, P-04
848873-95-0, Theralux 848873-96-1, PBI-1402 848873-97-2, SRL-172
848873-98-3, CDA-II 848873-99-4, SDX-101 848874-01-1, SN-4071
848874-02-2, Urocidin 849146-37-8, CTP-37 849146-41-4, Pentrix
849146-42-5, ISF-154 849148-55-6, Norelin 849148-82-9, TransMID-107
849148-97-6, MGV 849149-00-4, GMK 851343-54-9, 5-
Hydroxymethyl-discodermolide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human protein IAP (inhibitor of apoptosis protein) nucleobase
oligomers, including dsRNA, shRNA, and siRNA, and their use for
enhancing apoptosis in cancer therapy)

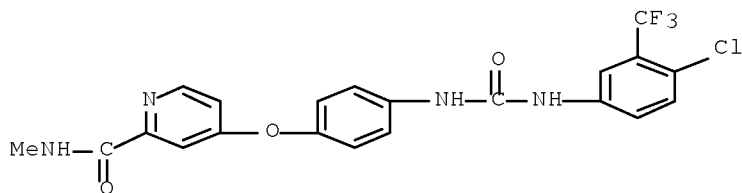
L110 ANSWER 7 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:409357 HCAPLUS Full-text
DOCUMENT NUMBER: 142:457052
TITLE: Sequences of antisense IAP (inhibitor of apoptosis

protein) oligomers and their use for treatment of
proliferative diseases with a chemotherapeutic agent
INVENTOR(S): Lacasse, Eric; McManus, Daniel; Durkin, Jon P.
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|--|----------|------------------|----------------|
| WO 2005042030 | A1 | 20050512 | WO 2004-CA1900 | 20041029 <-- |
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| US 20050119217 | A1 | 20050602 | US 2004-975790 | 20041028 <-- |
| AU 2004284855 | A1 | 20050512 | AU 2004-284855 | 20041029 <-- |
| CA 2542884 | A1 | 20050512 | CA 2004-2542884 | 20041029 <-- |
| EP 1691842 | A1 | 20060823 | EP 2004-789807 | 20041029 <-- |
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| BR 2004015779 | A | 20061226 | BR 2004-15779 | 20041029 <-- |
| CN 1901939 | A | 20070124 | CN 2004-80039601 | 20041029 <-- |
| JP 2007509861 | T | 20070419 | JP 2006-537023 | 20041029 <-- |
| MX 2006PA04920 | A | 20070216 | MX 2006-PA4920 | 20060502 <-- |
| IN 2006MN00614 | A | 20070420 | IN 2006-MN614 | 20060526 <-- |
| NO 2006002420 | A | 20060731 | NO 2006-2420 | 20060529 <-- |
| PRIORITY APPLN. INFO.: | | | US 2003-516263P | P 20031030 <-- |
| | | | WO 2004-CA1900 | W 20041029 |
| AB | The invention claims the use of an antisense oligomer to human XIAP, IAP-1 or IAP-2 genes and a chemotherapeutic agent, and compns. and kits thereof, for the treatment of proliferative diseases. The invention further claims sequences for nucleobase oligomers that are antisense IAP (inhibitor of apoptosis protein) oligomers. The antisense IAP nucleobase oligomers specifically hybridize with polynucleotides encoding an IAP and reduce the amount of an IAP protein produced in a cell. Thus by reducing the IAP protein, the invention provides methods for inducing cancer cells to undergo apoptosis and for overriding anti-apoptotic signals in cancer cells. As an example of the invention, mice with s.c. H460 human lung carcinoma xenografts were injected intratumorally with XIAP antisense mixed-base 2'-O-Me RNA oligonucleotides (C5 and/or G4) and the drug vinorelbine. At the end of the 24 d treatment period, the mean relative tumor growth was reduced .apprx.70% in treated mice. The inhibition of tumor growth was correlated with down-regulation of human XIAP protein expression and an increased number of dead cells. The mice did not show any signs of cytotoxicity such as body weight loss. | | | |
| IT | 284461-73-0, BAY-43-9006 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with | | | |

10/590724

chemotherapeutic agent)
RN 284461-73-0 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c
arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K048-00
ICS A61K031-7088; A61P035-00; A61K031-55
CC 1-6 (Pharmacology)
Section cross-reference(s): 3, 14
IT 199796-52-6, Taxoprexin 200484-11-3, CHS-828 201044-96-4, SB-T-1250
203258-60-0, Brostallicin 203923-89-1, BNP-1350 204005-46-9, SU5416
204205-90-3, D 24851 204318-14-9, Edotreotide 205923-56-4, C225
206873-63-4, Tariquidar 207862-44-0, KW-2170 209783-80-2, MS-275
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213819-48-8, CKD-602 216586-46-8, Virulizin 219923-05-4, ZD 6126
219989-84-1, Azaepothilone B 220578-59-6, Gemtuzumab zogamicin
220997-97-7, Diflomotecan 227619-96-7, CP-461 232925-18-7, Thymectacin
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333754-36-2, DJ-927 337308-14-2, MDX-H210 339151-96-1, MDX-447
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aminocarbonyldiscodermolide 358968-12-4, 2-EpiDiscodermolide
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ZD6474 446022-33-9, AG-2037 476172-88-0, 9(13)-Cyclodiscodermolide
492448-75-6, Oncophage 531508-98-2, GCS-100 543726-73-4, IMC-1C11
606967-38-8, MX6 623174-20-9, LU 223651 623174-20-9, ILX651
634599-18-1, WX-UK1 646067-94-9, EKB-509 665026-43-7, CV-247
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849148-55-6, Norelin 849148-82-9, TransMID-107 849148-97-6, MG
849149-00-4, GMK 851343-54-9, 5-Hydroxymethyl-discodermolide
851713-09-2, CDA 11 851713-35-4, 131I-TM 601
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sequences of antisense IAP (inhibitor of apoptosis protein) oligomers
and their use for treatment of proliferative diseases with
chemotherapeutic agent)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 8 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2005:346995 HCAPLUS Full-text
 DOCUMENT NUMBER: 142:411371
 TITLE: Preparation of pyrimidine derivatives as antitumor agents
 INVENTOR(S): Dixon, Julie A.; Nagarathnam, Dhanapalan; Zhang, Lei; Wang, Chunguang; Yi, Lin; Chen, Yuanwei; Chen, Jianqing; Bear, Brian; Brands, Michael; Hillisch, Alexander; Bierer, Donald; Wang, Ming; Fu, Wenlang; Hentemann, Martin F.; Bullion, Ann-Marie
 PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
 SOURCE: PCT Int. Appl., 276 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-------------------|-----------------|----------------|
| WO 2005035507 | A2 | 20050421 | WO 2004-US33430 | 20041008 <-- |
| WO 2005035507 | A3 | 20060831 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2542031 | A1 | 20050421 | CA 2004-2542031 | 20041008 <-- |
| EP 1689722 | A2 | 20060816 | EP 2004-809919 | 20041008 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| JP 2007508321 | T | 20070405 | JP 2006-534438 | 20041008 <-- |
| US 20050277640 | A1 | 20051215 | US 2005-78681 | 20050310 <-- |
| US 20070117817 | A1 | 20070524 | US 2006-573227 | 20060324 <-- |
| PRIORITY APPLN. INFO.: | | | US 2003-510804P | P 20031010 <-- |
| | | | WO 2004-US33430 | W 20041008 |
| OTHER SOURCE(S): | | MARPAT 142:411371 | | |
| GI | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = H, alkyl, cyclopropyl; R2 = alkyl, cyclopropyl, O-alkyl, etc.; R3 = H, halo; M = CH, N; L = carbonyl, O, (un)substituted-alkylenyl, etc.; J and Y independently = (un)substituted-aryl, -heteroaryl; A = halo, CF3, CN, etc.; m = 0-2] and their pharmaceutically acceptable salts, are prepared and disclosed as useful antitumor agents. Thus, e.g., II was prepared by etherification of 4-chloro-picoline with 4-aminophenol followed by amination of 4-chloro-6-phenylpyrimidin-2-amine (preparation given). The

10/590724

cytotoxic activity of I towards HCT116 cells was evaluated and selected compds. of the invention displayed IC50 values of less than or equal to 500 nM. I should prove useful in the treatment of hyperproliferative disorders.

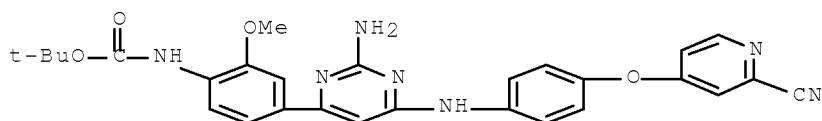
IT 850248-93-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrimidine derivs. as antitumor agents)

RN 850248-93-0 HCAPLUS

CN Carbamic acid, [4-[2-amino-6-[[4-[(2-cyano-4-pyridinyl)oxy]phenyl]amino]-4-pyrimidinyl]-2-methoxyphenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IC ICM C07D239-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

| | | | | | |
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| IT | 850246-99-0P | 850247-00-6P | 850247-01-7P | 850247-02-8P | 850247-03-9P |
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| 850249-92-2P | | | | |

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrimidine derivs. as antitumor agents)

L110 ANSWER 9 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:283363 HCAPLUS Full-text

DOCUMENT NUMBER: 142:329832

TITLE: Combination of a vegf receptor inhibitor with a chemotherapeutic agent

INVENTOR(S): Bold, Guido; Brueggen, Josef Bernhard; Huang, Jerry Min-Jian; Kinder, Frederick Ray, Jr.; Lane, Heidi; Latour, Elisabeth Jeanne; Manley, Paul William; Wood, Jeanette Marjorie

PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma GmbH

SOURCE: PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|--------------|
| ----- | --- | ----- | ----- | ----- |
| WO 2005027972 | A2 | 20050331 | WO 2004-EP10686 | 20040923 <-- |
| WO 2005027972 | A3 | 20051103 | | |
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| AU 2004273615 | A1 | 20050331 | AU 2004-273615 | 20040923 <-- |
| CA 2537991 | A1 | 20050331 | CA 2004-2537991 | 20040923 <-- |
| EP 1682181 | A2 | 20060726 | EP 2004-765542 | 20040923 <-- |
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| CN 1856327 | A | 20061101 | CN 2004-80027544 | 20040923 <-- |
| BR 2004014698 | A | 20061128 | BR 2004-14698 | 20040923 <-- |
| JP 2007505938 | T | 20070315 | JP 2006-527348 | 20040923 <-- |
| MX 2006PA03163 | A | 20060605 | MX 2006-PA3163 | 20060320 <-- |
| IN 2006CN00982 | A | 20070615 | IN 2006-CN982 | 20060322 <-- |

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| | | | | |
|------------------------|----|----------|-----------------|----------------|
| NO 2006001777 | A | 20060623 | NO 2006-1777 | 20060421 <-- |
| US 20080085902 | A1 | 20080410 | US 2007-573163 | 20070228 <-- |
| PRIORITY APPLN. INFO.: | | | US 2003-505250P | P 20030923 <-- |
| | | | WO 2004-EP10686 | W 20040923 |

OTHER SOURCE(S): MARPAT 142:329832

AB The present invention relates to a combination therapy for treating patients suffering from proliferative diseases or diseases associated with persistent angiogenesis. The patient is treated with: (a) a VEGF inhibitor compound; and (b) one or more chemotherapeutic agents selected from the group consisting of: an aromatase inhibitor; an anti-estrogen, an anti-androgen (especially in the case of prostate cancer) or a gonadorelin agonist; a topoisomerase I inhibitor or a topoisomerase II inhibitor; a microtubule active agent, an alkylating agent, an anti-neoplastic anti-metabolite or a platin compound; a compound targeting/decreasing a protein or lipid kinase activity or a protein or lipid phosphatase activity, a further anti-angiogenic compound or a compound which induces cell differentiation processes. The patient is treated with : (a) a VEGF inhibitor compound; and (b) one or more chemotherapeutic agents selected from the group consisting of : a bradykinin 1 receptor or an angiotensin II antagonist ; a cyclooxygenase inhibitor , a bisphosphonate , a heparanase inhibitor (prevents heparan sulfate degradation) , e.g. , PI-88 , a biol. response modifier, preferably a lymphokine or interferons , e.g., interferon γ , an ubiquitination inhibitor, or an inhibitor which blocks anti-apoptotic pathways ; an inhibitor of Ras oncogenic isoforms or a farnesyl transferase inhibitor ; a telomerase inhibitor , e.g. , telomestatin ; a protease inhibitor, a matrix metalloproteinase inhibitor , a methionine aminopeptidase inhibitor , e.g. , bengamide or a derivative thereof , or a proteasome inhibitor , e. g. , PS-341. The patient is treated with : (a) a VEGF inhibitor compound (b) one or more chemotherapeutic agents selected from the group consisting of : agents used in the treatment of hematol. malignancies or FMS-like tyrosine kinase inhibitors ; an HSP90 inhibitors ; HDAC inhibitors ; mTOR inhibitors ; somatostatin receptor antagonists ; integrin antagonists ; anti-leukemic compds. ; tumor cell damaging approaches such as ionizing radiation EDG binders ; anthranilic acid amide class of kinase inhibitors ; ribonucleotide reductase inhibitors ; S-adenosylmethionine decarboxylase inhibitors ; antibodies against VEGF or VEGFR ; photodynamic therapy ; angiostatic steroids ; implants containing corticosteroids ; AT1 receptor antagonists ; ACE inhibitors.

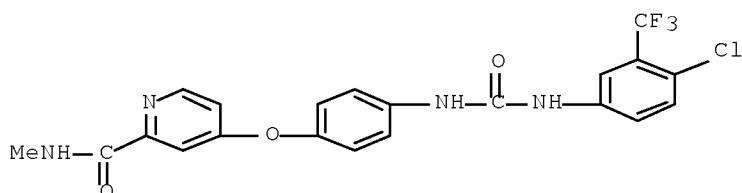
IT 284461-73-0, BAY43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination of vegf receptor inhibitor with chemotherapeutic agent)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c
arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K045-06
ICS A61K031-502

CC 1-6 (Pharmacology)
 Section cross-reference(s): 63
 IT 51-21-8, 5-FU 64-86-8D, Colchicine, derivs. 147-94-4, Ara-C
 12772-57-5, Radicicol 30562-34-6, Geldanamycin 33515-09-2, Gonadorelin
 40391-99-9, Pamidronic acid 53123-88-9, Rapamycin 75706-12-6, SU101
 75747-14-7, 17AAG 107868-30-4, Exemestane 112809-51-5, Letrozole
 118072-93-8, Zoledronic acid 120511-73-1, Anastrozole 120685-11-2,
 PKC412 127943-53-7, Discodermolide 152459-95-5, Imatinib
 159351-69-6, RAD 001 162011-90-7, Rofecoxib 162635-04-3, CCI-779
 169590-42-5, Celecoxib 169944-35-8, Bisulfan 179324-69-7, PS-341
 180288-69-1, Trastuzumab 181695-72-7, Valdecoxib 184475-35-2,
 Gefitinib 185077-23-0, PI 88 212141-54-3 212631-79-3, PD184352
 220064-45-9, GFB 111 220127-57-1, Imatinib mesylate 220991-20-8,
 Lumiracoxib 252916-29-3, SU6668 260415-63-2, PD173955
 284461-73-0, BAY43-9006 387867-13-2, MLN518 404950-80-7
 404951-53-7 572924-54-0, AP 23573
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (combination of vegf receptor inhibitor with chemotherapeutic agent)

L110 ANSWER 10 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:283298 HCAPLUS Full-text
 DOCUMENT NUMBER: 142:349042
 TITLE: Combinations of chlorpromazine compounds and
 antiproliferative drugs for the treatment of neoplasms
 INVENTOR(S): Lee, Margaret S.; Nichols, James M.; Zhang, Yanzhen;
 Keith, Curtis
 PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
 SOURCE: PCT Int. Appl., 65 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 7
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------|--|----------|------------------|--------------|
| WO 2005027842 | A2 | 20050331 | WO 2004-US30368 | 20040916 <-- |
| WO 2005027842 | A3 | 20051222 | | |
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KR 2007012618 A 20070126 KR 2006-707244 20060414 <--
 PRIORITY APPLN. INFO.: US 2003-504310P P 20030918 <--
 WO 2004-US30368 W 20040916

OTHER SOURCE(S): MARPAT 142:349042

AB The invention discloses a method for treating a patient having a cancer or other neoplasm by administering chlorpromazine or a chlorpromazine analog and an antiproliferative agent simultaneously or within 14 days of each other in amts. sufficient to treat the patient.

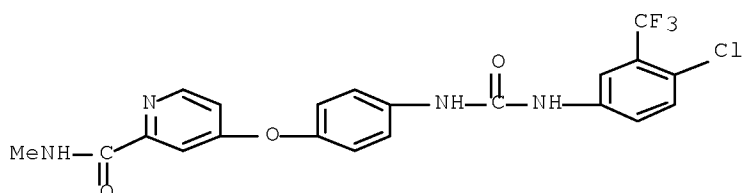
IT 284461-73-0, BAY-43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(chlorpromazine compound-antiproliferative drug antitumor combination)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c
 arboxyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K

CC 1-6 (Pharmacology)

IT 189752-49-6, Motexafin 191732-72-6, Revimid 192185-72-1, Tipifarnib
 192573-38-9, RPR 109881A 193275-84-2, Lonafarnib 195533-53-0, T 138067
 195612-80-7, Galarubicin 196488-72-9, Ranpirnase 199796-52-6,
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 849146-40-3, Synchrovax 849146-41-4, Pentrix 849146-42-5, ISF 154

10/590724

849148-55-6, Norelin 849148-82-9, TransMID 107 849148-97-6, MGW
 849149-00-4, GMK (immunomodulator)
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (chlorpromazine compound-antiproliferative drug antitumor combination)

L110 ANSWER 11 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:182644 HCAPLUS Full-text

DOCUMENT NUMBER: 142:280215

TITLE: Preparation of heteroaryl-substituted diarylureas as tyrosine kinase inhibitors

INVENTOR(S): Hoelzemann, Guenter; Ackermann, Karl-August; Staehle, Wolfgang; Jonczyk, Alfred; Rautenberg, Wilfried; Mitjans, Francesc; Rosell-Vives, Elisabet; Adan, Jaume; Soler, Marta; Crassier, Helene

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 72 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

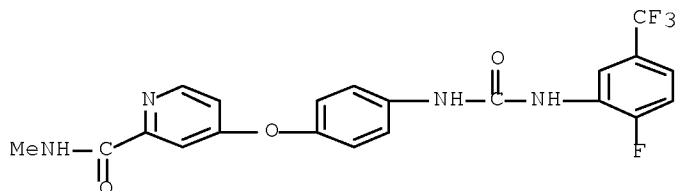
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|------------------|----------------|
| WO 2005019192 | A1 | 20050303 | WO 2004-EP7224 | 20040702 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10334663 | A1 | 20050310 | DE 2003-10334663 | 20030730 <-- |
| AU 2004266781 | A1 | 20050303 | AU 2004-266781 | 20040702 <-- |
| CA 2533963 | A1 | 20050303 | CA 2004-2533963 | 20040702 <-- |
| EP 1651626 | A1 | 20060503 | EP 2004-763077 | 20040702 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| JP 2007500136 | T | 20070111 | JP 2006-521413 | 20040702 <-- |
| US 20060241301 | A1 | 20061026 | US 2006-566351 | 20060130 <-- |
| PRIORITY APPLN. INFO.: | | | DE 2003-10334663 | A 20030730 <-- |
| | | | WO 2004-EP7224 | W 20040702 |
| AB | Twenty-eight title compds. were claimed. Thus, 5-(4-aminophenoxy)benzo-1,2,5-thiadiazole (preparation given), 2-fluoro-5-trifluoromethylphenyl isocyanate, and Et3N were stirred in CH2Cl2 to give 1[4-(benzo-1,2,5-thiadiazol-5-yloxy)phenyl]-3-(2-fluoro-5-trifluoromethylphenyl)urea as the trifluoroacetate. The latter inhibited TIE-2 and RAF kinase with IC50 = 57 nM and 220 nM, resp. | | | |
| IT | 847054-10-8P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (claimed compound; preparation of heteroaryl-substituted diarylureas as tyrosine kinase inhibitors) | | | |
| RN | 847054-10-8 HCAPLUS | | | |

10/590724

CN 2-Pyridinecarboxamide, 4-[4-[[[2-fluoro-5-(trifluoromethyl)phenyl]amino]c
arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D285-14
ICS C07D213-81; C07D213-70; C07D319-18; C07D277-64; C07D307-86;
C07D317-64; C07D213-69; C07D235-32; C07D471-04; C07D209-08;
A61P035-00; A61K031-435; A61K031-4745; A61K031-4184
CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT 847054-10-8P 847054-11-9P 847054-12-0P 847054-13-1P
847054-14-2P 847054-15-3P 847054-16-4P 847054-18-6P 847054-20-0P
847054-22-2P 847054-24-4P 847054-26-6P 847054-28-8P 847054-30-2P
847054-31-3P 847054-32-4P 847054-33-5P 847054-34-6P 847054-35-7P
847054-36-8P 847054-37-9P 847054-38-0P 847054-39-1P 847054-40-4P
847054-41-5P 847054-42-6P 847054-43-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(claimed compound; preparation of heteroaryl-substituted diarylureas as
tyrosine kinase inhibitors)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 12 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:141055 HCAPLUS Full-text
DOCUMENT NUMBER: 142:240466
TITLE: Preparation of piperazinylbenzocycloheptapyridines as
farnesyl protein transferase inhibitors useful as
antitumor agents.
INVENTOR(S): Zhu, Hugh Y.; Cooper, Alan B.; Desai, Jagdish A.;
Wang, James J.-S.; Rane, Dinanath F.; Doll, Ronald J.;
Njoroge, F. George; Girijavallabhan, Viyyoor M.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|--------------|
| WO 2005014577 | A1 | 20050217 | WO 2004-US25042 | 20040804 <-- |
| WO 2005014577 | A9 | 20060323 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

10/590724

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
 SN, TD, TG

| | | | | |
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| AU 2004263493 | A1 | 20050217 | AU 2004-263493 | 20040804 <-- |
| CA 2535210 | A1 | 20050217 | CA 2004-2535210 | 20040804 <-- |
| US 20050059672 | A1 | 20050317 | US 2004-911340 | 20040804 <-- |
| EP 1660477 | A1 | 20060531 | EP 2004-779960 | 20040804 <-- |

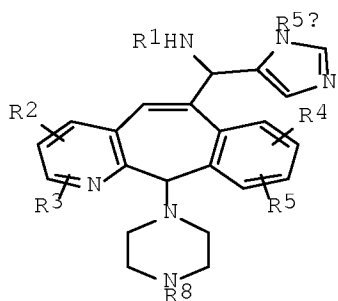
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

| | | | | |
|----------------|---|----------|------------------|--------------|
| BR 2004013384 | A | 20061017 | BR 2004-13384 | 20040804 <-- |
| CN 1863792 | A | 20061115 | CN 2004-80029384 | 20040804 <-- |
| JP 2007501791 | T | 20070201 | JP 2006-522672 | 20040804 <-- |
| IN 2006CN00459 | A | 20070518 | IN 2006-CN459 | 20060203 <-- |
| MX 2006PA01483 | A | 20060515 | MX 2006-PA1483 | 20060207 <-- |
| NO 2006001077 | A | 20060505 | NO 2006-1077 | 20060306 <-- |

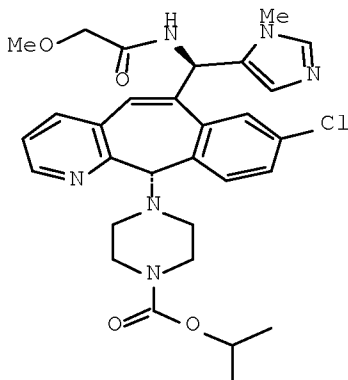
PRIORITY APPLN. INFO.:

| | | |
|-----------------|---|--------------|
| US 2003-493269P | P | 20030807 <-- |
| US 2003-498509P | P | 20030828 <-- |
| WO 2004-US25042 | W | 20040804 |

OTHER SOURCE(S): CASREACT 142:240466; MARPAT 142:240466
 GI



I



II

AB Title compds. [I; R1 = R9X(CR6R7)nCO, R10O2C; n = 1-6; X = O, S, N; R2-R5 = H, Br, Cl, F; R5a = H, alkyl, cycloalkyl; R6, R7 = H, alkyl; R6R7C = C3-7 cycloalkyl; R8 = R11O2C, R11SO2, R12R11aNCO, R21R22R46CO; R9 = alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, etc.; R10 = substituted aryl, heteroaryl, cycloalkyl, alkenyl, alkynyl, etc.; R11 = (substituted) alkyl, aryl, cycloalkyl, heteroaryl, heterocycloalkyl; R11a = H, OH, (substituted) alkyl, aryl, cycloalkyl, heteroaryl, heterocycloalkyl, etc.; R12 = H, alkyl, (substituted) piperidinyl, alkylpiperidinyl; R21, R22, R46 = H, alkyl, (substituted) aryl, cycloalkyl, heteroaryl, piperidinyl, etc.], were prepared Thus, title compound (II) was prepared in several steps from 8-chloro-5,6-dihydro-11H-

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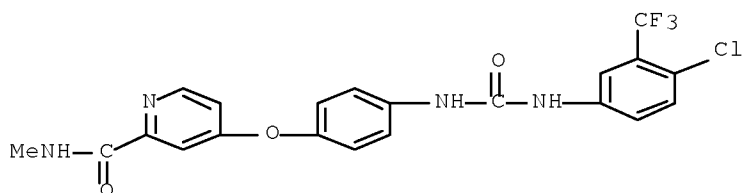
benzo[5,6]cyclohepta[1,2-b]pyridin-11-one. I inhibited FPTase with IC50 in the range of <0.5 nM to 5 nM.

IT 284461-73-0, Bay 43-9006

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of piperazinylbenzocycloheptapyridines as farnesyl protein transferase inhibitors useful as antitumor agents)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c
arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D401-06

ICS C07D401-14; A61K031-415; A61P035-00

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 50-35-1, Thalidomide 566-48-3, Formestane 9034-40-6D, Lhrh, analogs
10540-29-1, Tamoxifen 15663-27-1, Cisplatin 33069-62-4, Taxol
41575-94-4, Carboplatin 53714-56-0, Leuporelin 65807-02-5, Goserelin
84449-90-1, Raloxifene 95058-81-4, Gemcitabine 102676-47-1, Fadrozole
107868-30-4, Exemestane 112809-51-5, Letrozole 114977-28-5, Taxotere
120511-73-1, Anastrozole 129453-61-8, Fulvestrant 174722-31-7,
Rituximab 179324-69-7, Bortezomib 180288-69-1, Herceptin
182167-02-8, Acolbifene 183319-69-9, Osi-774 183321-74-6, Erlotinib
184475-35-2, Iressa 190977-41-4, Genasense 204005-46-9, Su5416
205923-56-4, c225 216974-75-3, Bevacizumab 220127-57-1, Gleevec
284461-73-0, Bay 43-9006 339177-26-3, ABX-EGF 543726-73-4, IMC
1C11 543726-78-9, SU 6688

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of piperazinylbenzocycloheptapyridines as farnesyl protein transferase inhibitors useful as antitumor agents)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 13 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:99470 HCAPLUS Full-text

DOCUMENT NUMBER: 142:197889

TITLE: Fluoro substituted omega-carboxyaryl diphenyl urea for
treatment of raf, VEGFR, PDGFR, p38 and flt-3
kinase-mediated diseases

INVENTOR(S): Dumas, Jacques; Boyer, Stephen; Riedl, Bernd; Wilhelm,
Scott

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

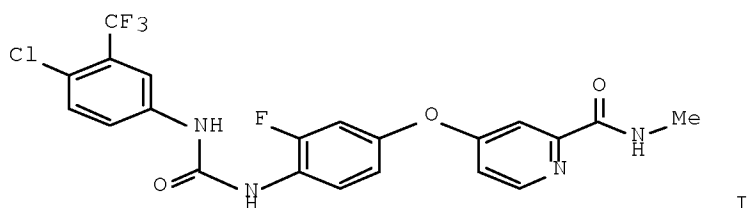
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|---------------------|----------------|
| WO 2005009961 | A2 | 20050203 | WO 2004-US23500 | 20040722 <-- |
| WO 2005009961 | A3 | 20050331 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004259760 | A1 | 20050203 | AU 2004-259760 | 20040722 <-- |
| CA 2532865 | A1 | 20050203 | CA 2004-2532865 | 20040722 <-- |
| US 20050038080 | A1 | 20050217 | US 2004-895985 | 20040722 <-- |
| EP 1663978 | A2 | 20060607 | EP 2004-786091 | 20040722 <-- |
| EP 1663978 | B1 | 20071128 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| BR 2004012219 | A | 20060822 | BR 2004-12219 | 20040722 <-- |
| CN 1856469 | A | 20061101 | CN 2004-80021091 | 20040722 <-- |
| JP 2006528196 | T | 20061214 | JP 2006-521221 | 20040722 <-- |
| ES 2297490 | T3 | 20080501 | ES 2004-786091 | 20040722 <-- |
| MX 2006PA00860 | A | 20060720 | MX 2006-PA860 | 20060123 <-- |
| IN 2006DN00402 | A | 20070824 | IN 2006-DN402 | 20060123 <-- |
| NO 2006000870 | A | 20060407 | NO 2006-870 | 20060222 <-- |
| PRIORITY APPLN. INFO.: | | | US 2003-489102P | P 20030723 <-- |
| | | | US 2004-540326P | P 20040202 |
| | | | WO 2004-US23500 | W 20040722 |
| OTHER SOURCE(S): | | | CASREACT 142:197889 | |
| GI | | | | |



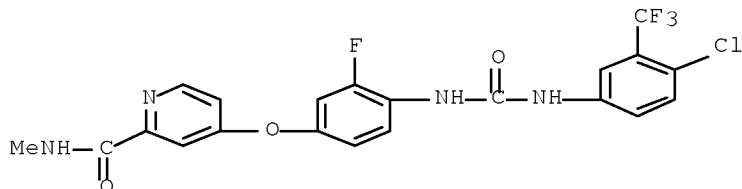
- AB Title compound I is prepared I and salts thereof is prepared in several steps from 3-fluoro-4-nitrophenol, 4-chloro-N-methylpyridine-2-carboxamide and 4-chloro-3-(trifluoromethyl)phenylisocyanate. I inhibits PDGFR tyrosine kinase with IC₅₀ = 83 nM. I is useful for the treatment of, e.g., inflammation and as an antiproliferative agent.
- IT 755037-03-7P, 4-[4-[N'-(4-Chloro-3-trifluoromethylphenyl)ureido]-3-fluorophenoxy]pyridine-2-carboxylic acid methylamide
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

10/590724

(fluoro substituted omega-carboxyaryl di-Ph urea for treatment of raf,
VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases)

RN 755037-03-7 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c
arbonyl]amino]-3-fluorophenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D213-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

IT 755037-03-7P, 4-[4-[N'-(4-Chloro-3-trifluoromethylphenyl)ureido]-3-
fluorophenoxy]pyridine-2-carboxylic acid methylamide

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); RACT (Reactant or reagent); USES (Uses)

(fluoro substituted omega-carboxyaryl di-Ph urea for treatment of raf,
VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases)

IT 835621-07-3P 835621-08-4P 835621-09-5P

835621-10-8P, [4-[N'-(4-Chloro-3-trifluoromethylphenyl)ureido]-3-
fluorophenoxy]pyridine-2-carboxylic acid amide 835621-11-9P

835621-12-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(fluoro substituted omega-carboxyaryl di-Ph urea for treatment of raf,
VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases)

L110 ANSWER 14 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:99357 HCAPLUS Full-text

DOCUMENT NUMBER: 142:198088

TITLE: Preparation of pyrimidinecarboxamides,
pyrimidinylcarbamates and related compounds as
inhibitors of T cell activation for the treatment of
inflammatory diseases

INVENTOR(S): Nunes, Joseph J.; Zhu, Xiaotian; Amouzegh, Patricia;
Ghiron, Chiara; Johnston, David N.; Power, Eoin
Christopher

PATENT ASSIGNEE(S): Amgen Inc., USA

SOURCE: PCT Int. Appl., 462 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|--------------|
| ----- | ---- | ----- | ----- | ----- |
| WO 2005009443 | A1 | 20050203 | WO 2004-US20243 | 20040624 <-- |

10/590724

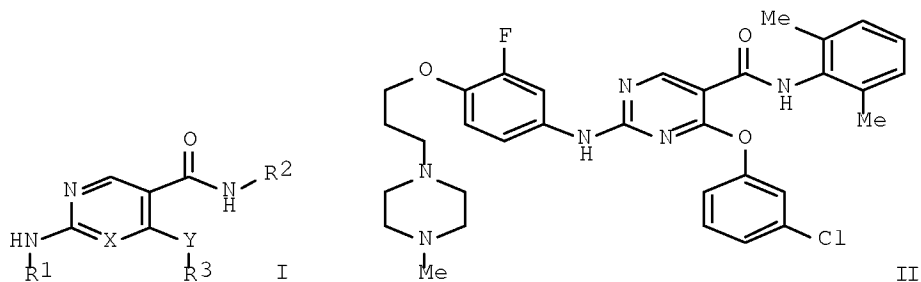
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|----------------|----|----------|-----------------|--------------|
| US 20050209221 | A1 | 20050922 | US 2004-875896 | 20040623 <-- |
| AU 2004258862 | A1 | 20050203 | AU 2004-258862 | 20040624 <-- |
| CA 2529734 | A1 | 20050203 | CA 2004-2529734 | 20040624 <-- |
| EP 1648464 | A1 | 20060426 | EP 2004-777011 | 20040624 <-- |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

PRIORITY APPLN. INFO.:
US 2003-482375P P 20030624 <--
US 2004-875896 A 20040623
WO 2004-US20243 W 20040624

OTHER SOURCE(S): MARPAT 142:198088
GI



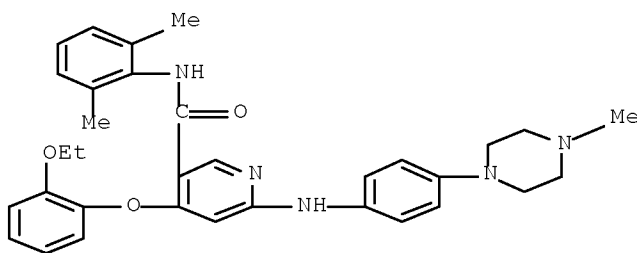
AB Pyrimidine and pyridine carboxamides I [wherein X = N or CH; Y = NH, O or S; R¹ - R³ = certain (un)substituted monocyclic or bicyclic ring; or pharmaceutically acceptable salts thereof] as well as pyrimidinylcarbamates were prepared as inhibitors of T cell activation. For example, 2,4-dichloropyrimidine-5-carbonyl chloride, obtained by globally chlorination of uracil-5-carboxylic acid monohydrate with PCl₅ in POCl₃, underwent amidation with 2,6-dimethylaniline, followed by etherification with 3-chlorophenol and subsequent amination with 3-fluoro-4-(3-(4-methyl-1-piperazinyl)propoxy)aniline to give pyrimidinecarboxamide II. Representative compds. I exhibited inhibition with IC₅₀ values of <10 μM in the LCK-homogeneous time resolved fluorescent kinase assay. Therefore, I and pharmaceutical compns. thereof are useful in the treatment of many diseases such as inflammation.

IT 835641-38-8P, N-(2,6-Dimethylphenyl)-4-[[2-(ethyloxy)phenyl]oxy]-6-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-3-pyridinecarboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(inhibitor; preparation of pyrimidinecarboxamides and pyrimidinylcarbamates as inhibitors of T cell activation for treatment of inflammatory diseases)

RN 835641-38-8 HCAPLUS

CN 3-Pyridinecarboxamide, N-(2,6-dimethylphenyl)-4-(2-ethoxyphenoxy)-6-[[4-(4-methyl-1-piperazinyl)phenyl]amino]- (CA INDEX NAME)



IC ICM A61K031-506

ICS A61K031-505; C07D239-46; C07D239-48

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

IT 835641-38-8P, N-(2,6-Dimethylphenyl)-4-[[2-(ethyloxy)phenyl]oxy]-6-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-3-pyridinecarboxamide
 835641-39-9P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-40-2P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide
 835641-41-3P, 2-[[3,5-Bis(methyloxy)-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-42-4P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-(methyloxy)-4-[[2-(4-methyl-1-piperazinyl)ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-43-5P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-(methyloxy)-4-(4-methyl-1-piperazinyl)phenyl]amino]-5-pyrimidinecarboxamide 835641-44-6P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-[(difluoromethyl)oxy]-4-(4-methyl-1-piperazinyl)phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-45-7P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-chloro-4-[4-(1-methylethyl)-1-piperazinyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide
 835641-46-8P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[2-(methyloxy)-4-[(1-pyrrolidinyl)carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide 835641-47-9P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[(1-pyrrolidinyl)carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide
 835641-48-0P 835641-49-1P, 4-[[3-(Acetylaminophenyl]oxy]-2-[[4-(diethylamino)butyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide
 835641-50-4P, 4-[[3-(Acetylaminophenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-pyrimidinecarboxamide
 835641-51-5P, 4-[[2-Chloro-4-(1-pyrrolidinylcarbonyl)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-52-6P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835641-53-7P, N-(2,6-Dimethylphenyl)-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]ami

no]-5-pyrimidinecarboxamide 835641-54-8P, 2-[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835641-55-9P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835641-56-0P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835641-57-1P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835641-58-2P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[3-[(1R)-1-methylpropyl]amino]-3-oxopropyl]phenyl]oxy]-5-pyrimidinecarboxamide 835641-59-3P, 2-[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[3-[(1R)-1-methylpropyl]amino]-3-oxopropyl]phenyl]oxy]-5-pyrimidinecarboxamide 835641-60-6P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[3-[(1R)-1-methylpropyl]amino]-3-oxopropyl]phenyl]oxy]-5-pyrimidinecarboxamide 835641-61-7P 835641-62-8P 835641-63-9P, 4-[[4-[4-(Diethylamino)-4-oxobutyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-64-0P, 4-[[4-[4-(Diethylamino)-4-oxobutyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-65-1P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-[(2-pyridinyl)methyl]-5-pyrimidinecarboxamide 835641-66-2P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-N-[(2-pyridinyl)methyl]-5-pyrimidinecarboxamide 835641-67-3P, 2-[[3-Chloro-4-[4-(1-methylethyl)-1-piperazinyl]phenyl]amino]-4-[(2,2-dimethyl-2,3-dihydrobenzo[b]furan-7-yl)oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-68-4P, 2-[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-4-[(2,2-dimethyl-2,3-dihydrobenzo[b]furan-7-yl)oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-69-5P, 4-[(2,2-Dimethyl-2,3-dihydrobenzo[b]furan-7-yl)oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835641-70-8P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[(2,2-dimethyl-2,3-dihydrobenzo[b]furan-7-yl)oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-71-9P, 4-[(2,2-Dimethyl-2,3-dihydrobenzo[b]furan-7-yl)oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-72-0P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-[(1S)-1-phenylethyl]-5-pyrimidinecarboxamide 835641-73-1P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-N-[(1S)-1-phenylethyl]-5-pyrimidinecarboxamide 835641-74-2P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(4-fluorophenyl)-5-pyrimidinecarboxamide 835641-75-3P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(4-fluorophenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-76-4P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2-fluorophenyl)-5-pyrimidinecarboxamide 835641-77-5P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2-fluorophenyl)-2-[[3-fluoro-4-[[3-

(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide
835641-78-6P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,4,6-trimethylphenyl)-5-pyrimidinecarboxamide 835641-79-7P,
4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-N-(2,4,6-trimethylphenyl)-5-pyrimidinecarboxamide 835641-80-0P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,4,6-trifluorophenyl)-5-pyrimidinecarboxamide 835641-81-1P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-N-(2,4,6-trifluorophenyl)-5-pyrimidinecarboxamide 835641-82-2P, 4-[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-83-3P, 4-[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-84-4P, 2-[[4-[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-4-[[4-[2-(diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-85-5P, 4-[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-86-6P, 4-[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-87-7P, 4-[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835641-88-8P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-[2-(diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-89-9P, N-(2,6-Dimethylphenyl)-4-[[2-(methyloxy)-4-[3-oxo-3-(1-pyrrolidinyl)propyl]phenyl]oxy]-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-pyrimidinecarboxamide 835641-90-2P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-91-3P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-92-4P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-93-5P, 2-[[4-[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-94-6P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-95-7P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-96-8P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-97-9P, 4-[[2-Chloro-4-[2-(diethylamino)ethyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-(4-methyl-1-piperazinyl)phenyl]amino]-5-pyrimidinecarboxamide 835641-98-0P, 4-[[2-Chloro-4-[2-(diethylamino)ethyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-[4-(1-methylethyl)-1-piperazinyl]phenyl]amino]-5-

pyrimidinecarboxamide 835641-99-1P, 4-[[2-Chloro-4-[2-(diethylamino)ethyl]phenyl]oxy]-2-[[4-[4-[3-(dimethylamino)propyl]-1-piperazinyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide
835642-00-7P, 2-[[4-[[2-(Dimethylamino)ethyl]amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-propylphenyl]oxy]-5-pyrimidinecarboxamide 835642-01-8P, 2-[[3-[[2-(Dimethylamino)ethyl]amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-propylphenyl]oxy]-5-pyrimidinecarboxamide
835642-02-9P, 2-[[4-[[2-(Dimethylamino)ethyl]amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(ethyloxy)phenyl]oxy]-5-pyrimidinecarboxamide
835642-03-0P, 2-[[3-[[2-(Dimethylamino)ethyl]amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(ethyloxy)phenyl]oxy]-5-pyrimidinecarboxamide
835642-04-1P, 4-[[2-Chloro-4-[2-oxo-2-(1-pyrrolidinyl)ethyl]phenyl]oxy]-2-[[4-[[2-(diethylamino)ethyl]amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-05-2P, 4-[[2-Chloro-4-[2-oxo-2-(1-pyrrolidinyl)ethyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide
835642-06-3P, 4-[[2-Chloro-4-[2-oxo-2-(1-pyrrolidinyl)ethyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide
835642-07-4P, 2-[[4-[[2-(Diethylamino)ethyl]amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[(1-pyrrolidinyl)carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide 835642-08-5P, 2-[[3,4-Bis(methyloxy)-5-[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[(1-pyrrolidinyl)carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide 835642-09-6P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[(1-pyrrolidinyl)carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide 835642-10-9P, 2-[[3,4-Bis(methyloxy)-5-[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-11-0P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-12-1P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide
835642-13-2P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-14-3P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[1-methyl-3-piperidinyl]methyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide
835642-15-4P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-16-5P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[4-[[2-(diethylamino)ethyl]amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-17-6P, 2-[[3,4-Bis(methyloxy)-5-[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[4-[[1-methylethyl]amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-18-7P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-[[1-methylethyl]amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-19-8P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[4-[[1-methylethyl]amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-20-1P, N-(2,6-Dimethylphenyl)-4-[[4-[[1-

methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide
835642-21-2P, 2-[[4-[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[4-[[1-methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-22-3P,
N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[4-[[1-methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-23-4P,
N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[4-[[1-methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-24-5P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[4-[[1-methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-25-6P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-[[cyclopentylamino]carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-26-7P,
4-[[4-[[Cyclopentylamino]carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-27-8P, 4-[[4-[[Cyclopentylamino]carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-28-9P, 4-[[4-[[Cyclopentylamino]carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-29-0P, 4-[[4-[[Cyclopentylamino]carbonyl]-2-(methyloxy)phenyl]oxy]-2-[[4-[[2-(diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-30-3P, 4-[[4-[[Cyclopentylamino]carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-31-4P, 4-[[4-[[Cyclopentylamino]carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-32-5P, 4-[[4-[[Cyclopentylamino]carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835642-33-6P, 4-[[4-[[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-34-7P, 4-[[2-Chloro-4-[[4-(1-methylethyl)-1-piperazinyl]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-35-8P, 4-[[2-Chloro-4-[[4-(1-methylethyl)-1-piperazinyl]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-36-9P, 4-[[2-Chloro-4-[[4-(1-methylethyl)-1-piperazinyl]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-37-0P, 4-[[2-Chloro-4-[[4-(1-methylethyl)-1-piperazinyl]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-38-1P, 4-[[2-Chloro-4-[[4-(1-methylethyl)-1-piperazinyl]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835642-39-2P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-chloro-4-[[2-(methyloxy)ethyl]amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-40-5P, 2-[[4-[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-

dimethylphenyl)-4-[[4-[3-[4-(1-methylethyl)-1-piperazinyl]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-41-6P,
N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[4-(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[4-[3-[4-(1-methylethyl)-1-piperazinyl]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-42-7P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[4-[3-[4-(1-methylethyl)-1-piperazinyl]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-43-8P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-44-9P,
, 4-[[2-Chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-45-0P, 4-[[2-Chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-46-1P, 4-[[2-Chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-2-[[4-[[2-(diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-47-2P, 4-[[2-Chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-48-3P, 4-[[2-Chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[4-(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-49-4P, 4-[[2-Chloro-4-(4-morpholinylcarbonyl)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-50-7P, 4-[[2-Chloro-4-(4-morpholinylcarbonyl)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-51-8P, 4-[[2-Chloro-4-(4-morpholinylcarbonyl)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[4-(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-52-9P, 4-[[2-Chloro-4-[[4-(1-methylethyl)amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-53-0P, 4-[[2-Chloro-4-[[4-(1-methylethyl)amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-54-1P, 4-[[2-Chloro-4-[[4-(1-methylethyl)amino]carbonyl]phenyl]oxy]-2-[[4-[[2-(diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-55-2P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-chloro-4-[[4-(1-methylethyl)amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-56-3P, N-(2,6-Dimethylphenyl)-4-[(2-ethylimidazo[1,2-a]pyridin-8-yl)oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-57-4P, 2-[[4-[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-4-[[3-[3-(diethylamino)-3-oxopropyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-58-5P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[3-[3-(diethylamino)-3-oxopropyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-59-6P, 4-[[3-[3-(Diethylamino)-3-oxopropyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[4-(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-60-9P, 4-[[3-[3-(Diethylamino)-3-oxopropyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide

835642-61-0P, 4-[[3-[3-(Diethylamino)-3-oxopropyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-62-1P, 4-[[2-Chloro-4-(4-morpholinylcarbonyl)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835642-63-2P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dichloro-4-fluorophenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-64-3P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dichloro-4-fluorophenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-65-4P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(4-fluoro-2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-66-5P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(4-fluoro-2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-67-6P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-[(5-methyl-3-isoxazolyl)methyl]-5-pyrimidinecarboxamide 835642-68-7P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-N-[(5-methyl-3-isoxazolyl)methyl]-5-pyrimidinecarboxamide 835642-69-8P, 4-[[2-Chloro-4-[[2-(methyloxy)ethyl]amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-70-1P, 4-[[2-Chloro-4-[[2-(methyloxy)ethyl]amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-71-2P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-[(diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-72-3P, 4-[[4-[(Diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-73-4P, 4-[[4-[(Diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-2-[[4-[[2-(diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-74-5P, 4-[[4-[(Diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-75-6P, 4-[[4-[(Diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-76-7P, 4-[[4-[(Diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835642-77-8P, 4-[[4-[3-(Cyclopentylamino)-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-78-9P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[4-[3-[(1-methylethyl)amino]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-79-0P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[2-(methyloxy)-4-[3-[[2-(methyloxy)ethyl]amino]-3-oxopropyl]phenyl]oxy]-5-pyrimidinecarboxamide 835642-80-3P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[3-[[2-(methyloxy)ethyl]amino]-3-oxopropyl]phenyl]oxy]-5-pyrimidinecarboxamide 835642-81-4P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[4-[3-[(1-methylethyl)amino]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-

pyrimidinecarboxamide 835642-82-5P, 4-[[4-[3-(Cyclopentylamino)-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-83-6P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-[3-(cyclopentylamino)-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-84-7P, 4-[[4-[3-(Cyclopentylamino)-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-85-8P, 4-[[4-[3-(Cyclopentylamino)-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835642-86-9P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[4-[3-[(1-methylethyl)amino]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-87-0P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[4-[3-[(1-methylethyl)amino]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-88-1P, N-(2,6-Dimethylphenyl)-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-89-2P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-(4-morpholinyl)-2-oxoethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-90-5P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-(4-morpholinyl)-2-oxoethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-91-6P, N-(2,6-Dimethylphenyl)-4-[[2-(methyloxy)-4-[[2-(4-morpholinyl)-2-oxoethyl]oxy]phenyl]oxy]-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-92-7P, 2-[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[[2-(4-morpholinyl)-2-oxoethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-93-8P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[1-pyrrolidinyl]carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(inhibitor; preparation of pyrimidinecarboxamides and pyrimidinylcarbamates as inhibitors of T cell activation for treatment of inflammatory diseases)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 15 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:99319 HCAPLUS Full-text

DOCUMENT NUMBER: 142:172181

TITLE: Novel targets of protein kinase-inhibiting drugs for novel disease therapies

INVENTOR(S): Biggs, William H., III; Carter, Todd; Fabian, Miles A.; Lockhart, David J.; Zarrinkar, Patrick Parvis; Treiber, Daniel Kelly; Edeen, Phillip

PATENT ASSIGNEE(S): Ambit Biosciences Corporation, USA

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|--------------|
| WO 2005009367 | A2 | 20050203 | WO 2004-US23325 | 20040719 <-- |
| WO 2005009367 | A3 | 20050512 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|----------------|----|----------|----------------|--------------|
| US 20060234931 | A1 | 20061019 | US 2004-894877 | 20040719 <-- |
|----------------|----|----------|----------------|--------------|

| | | |
|------------------------|-----------------|----------------|
| PRIORITY APPLN. INFO.: | US 2003-488513P | P 20030717 <-- |
|------------------------|-----------------|----------------|

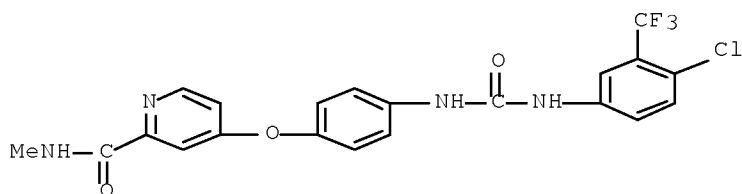
AB The invention is directed to the identification and use of addnl. targets of BIRB 796, imatinib mesylate, and BAY 43-9006. The new targets of BIRB 796, imatinib mesylate, and BAY 43-9006 can be used to screen for suitable therapeutic compds. Novel therapeutic and prophylactic uses for BIRB 796, imatinib mesylate, and BAY 43-9006 are disclosed. Protein targets of the drugs were identified using a phage-based competition assay using a panel of 69 proteins including 48 kinases.

IT 284461-73-0, BAY 43-9006

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel targets of protein kinase-inhibiting drugs for novel disease therapies)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K

CC 7-4 (Enzymes)

Section cross-reference(s): 1, 3

IT 220127-57-1, Imatinib mesylate 284461-73-0, BAY 43-9006
285983-48-4, BIRB 796

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel targets of protein kinase-inhibiting drugs for novel disease therapies)

L110 ANSWER 16 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:55204 HCAPLUS Full-text

DOCUMENT NUMBER: 142:134581

10/590724

TITLE: Preparation of malonamide derivatives useful as raf-kinase inhibitors

INVENTOR(S): Bruge, David; Buchstaller, Hans-Peter; Wiesner, Matthias; Finsinger, Dirk; Baumgarth, Manfred; Sirrenberg, Christian; Zenke, Frank; Amendt, Christiane; Grell, Matthias

PATENT ASSIGNEE(S): Merck Patent GmbH, Germany

SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2

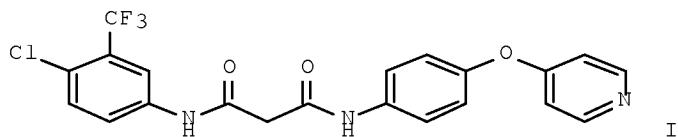
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-------------------|-----------------|----------------|
| WO 2005005389 | A2 | 20050120 | WO 2004-EP6573 | 20040618 <-- |
| WO 2005005389 | A3 | 20050324 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004255566 | A1 | 20050120 | AU 2004-255566 | 20040618 <-- |
| CA 2531485 | A1 | 20050120 | CA 2004-2531485 | 20040618 <-- |
| EP 1641759 | A2 | 20060405 | EP 2004-740026 | 20040618 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| JP 2007508238 | T | 20070405 | JP 2006-518009 | 20040618 <-- |
| US 20070213374 | A1 | 20070913 | US 2007-563830 | 20070125 <-- |
| PRIORITY APPLN. INFO.: | | | EP 2003-14556 | A 20030707 <-- |
| | | | WO 2004-EP6573 | W 20040618 |
| OTHER SOURCE(S): | | MARPAT 142:134581 | | |
| GI | | | | |



AB Malonamide derivs. of formula A-D-B [wherein: D is (un)substituted bivalent malonamide moiety; A and B are independently selected from (hetero)aryl derivs.], useful as raf-kinase inhibitors (no biol. data), were prepared For instance, malonamide derivative I was obtained via amidation of 3-[(4-chloro-3-trifluoromethylphenyl)amino]-2-oxo-propionic acid by 4-(4-pyridinyloxy)phenylamine with a yield of 57%.

IT 827029-05-0F

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

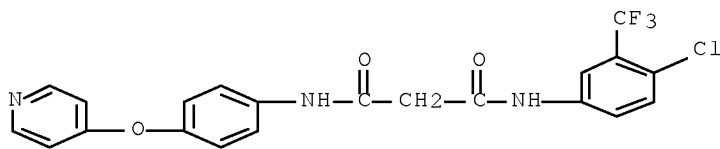
10/590724

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of malonamide derivs. useful as raf-kinase inhibitors)

RN 827029-05-0 HCAPLUS

CN Propanediamide, N1-[4-chloro-3-(trifluoromethyl)phenyl]-N3-[4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME)



IC ICM C07D213-00

CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 27, 63

IT 827029-05-0P 827029-06-1P 827029-07-2P 827029-08-3P
827029-09-4P 827029-10-7P 827029-11-8P 827029-22-1P
827029-23-2P 827029-24-3P 827029-25-4P
827029-26-5P 827029-27-6P 827029-28-7P
827029-29-8P 827029-30-1P 827029-31-2P
827029-32-3P 827029-33-4P 827029-34-5P
827029-35-6P 827029-36-7P 827029-37-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of malonamide derivs. useful as raf-kinase inhibitors)

L110 ANSWER 17 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:14200 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 142:86701

TITLE: Diaryl ureas for treatment of diseases mediated by PDGFR

INVENTOR(S): Wilhelm, Scott; Dumas, Jacques; Ladouceur, Gaetan; Lynch, Mark; Scott, William J.

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|--------------|
| WO 2005000284 | A2 | 20050106 | WO 2004-US15653 | 20040519 <-- |
| WO 2005000284 | A3 | 20050310 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, | | | |

10/590724

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

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|----------------|----|----------|-----------------|--------------|
| CA 2526636 | A1 | 20050106 | CA 2004-2526636 | 20040519 <-- |
| US 20050059703 | A1 | 20050317 | US 2004-848567 | 20040519 <-- |
| EP 1626714 | A2 | 20060222 | EP 2004-776037 | 20040519 <-- |
| EP 1626714 | B1 | 20070704 | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

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|----------------|----|----------|-----------------|--------------|
| JP 2006528986 | T | 20061228 | JP 2006-533210 | 20040519 <-- |
| AT 366108 | T | 20070715 | AT 2004-776037 | 20040519 <-- |
| ES 2288694 | T3 | 20080116 | ES 2004-776037 | 20040519 <-- |
| AT 384264 | T | 20080215 | AT 2004-752642 | 20040519 <-- |
| MX 2005PA12486 | A | 20060703 | MX 2005-PA12486 | 20051118 <-- |

PRIORITY APPLN. INFO.:

| | | |
|-----------------|---|--------------|
| US 2003-471735P | P | 20030520 <-- |
| US 2003-520399P | P | 20031117 <-- |
| US 2004-556062P | P | 20040325 |
| WO 2004-US15653 | W | 20040519 |

OTHER SOURCE(S): MARPAT 142:86701

AB The present invention provides methods for treating and/or preventing conditions and diseases in humans and other mammals that are associated with and/or mediated by signal transduction pathways comprising platelet-derived growth factor receptor (PDGFR), especially PDGFR- β , by administering diaryl ureas. The present invention also provides devices and methods for treating, ameliorating, preventing, or modulating restenosis following angioplastic surgery or other invasive procedures that affect or injure the vascular system, and graft rejection following transplantation of a donor tissue into a host, where a stent or other implantable device comprises an effective amount of diaryl ureas. For example, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]-2-fluorophenyl] urea, and N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]-2-chlorophenyl]urea showed an IC₅₀ of less than 10 μ M in a pPDGFR- β sandwich ELISA in AoSMC cells.

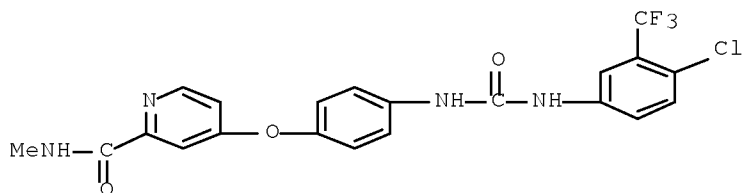
IT 284461-73-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(diaryl ureas for prevention and/or treatment of diseases mediated by platelet-derived growth factor receptor)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K031-00

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

IT 57-13-6D, Urea, diaryl derivs. 284461-73-0 284461-74-1
284461-80-9 284462-18-6 284462-19-7

10/590724

475207-59-1 583840-03-3 583840-04-4

755037-03-7 755037-03-7D, salts 755037-04-8

757229-80-4 819792-84-2 819792-85-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(diaryl ureas for prevention and/or treatment of diseases mediated by
platelet-derived growth factor receptor)

L110 ANSWER 18 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1313901 HCAPLUS Full-text

DOCUMENT NUMBER: 144:51598

TITLE: Preparation of amino-substituted pyrimidines as
antitumor agents

INVENTOR(S): Dixon, Julie A.; Nagarathnam, Dhanapalan; Zhang, Lei;
Wang, Chunguang; Yi, Lin; Chen, Yuanwei; Chen,
Jianqing; Bear, Brian R.; Brands, Michael; Hillisch,
Alexander; Bierer, Donald; Wang, Ming; Fu, Wenlang;
Hentemann, Martin F.; Bullion, Ann-Marie; Patel, Manoj

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 182 pp., Cont.-in-part of Appl.
No. PCT/US04/033430.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------|------|----------|-----------------|--------------|
| US 20050277640 | A1 | 20051215 | US 2005-78681 | 20050310 <-- |
| WO 2005035507 | A2 | 20050421 | WO 2004-US33430 | 20041008 <-- |
| WO 2005035507 | A3 | 20060831 | | |

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CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, YU, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-510804P P 20031010 <--
WO 2004-US33430 A2 20041008

OTHER SOURCE(S): CASREACT 144:51598; MARPAT 144:51598

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = H, alkyl, cyclopropyl; R2 = alkyl, cyclopropyl, O-alkyl,
etc.; R3 = H, halo; M = CH, N; L = carbonyl, O, (un)substituted alkylene,
etc.; J and Y independently = substituted aryl, heteroaryl; A = halo, CF3, CN,
etc.; m = 0-2] and their pharmaceutically acceptable salts, are prepared and
disclosed as useful antitumor agents. Thus, coupling 6-chloro-N4-(4-{[2-
(trifluoromethyl)pyridin-4-yl]oxy}phenyl)pyrimidine-2,4- diamine with 1,3-

10/590724

dimethylphenylboronic acid afforded 56% II which showed IC50 of 62 nM in test for cytotoxic activity on HCT-116 cells.

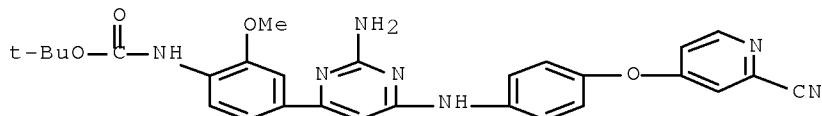
IT 850248-93-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino-substituted pyrimidines as antitumor agents)

RN 850248-93-0 HCAPLUS

CN Carbamic acid, [4-[2-amino-6-[[4-[(2-cyano-4-pyridinyl)oxy]phenyl]amino]-4-pyrimidinyl]-2-methoxyphenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IC ICM A61K031-5377

ICS A61K031-506; C07D413-14; C07D043-02

INCL 514235500; 514252140; 514256000; 544122000; 544295000; 544296000; 544329000

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, §3

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| | 850248-98-5P | 850248-99-6P | 850249-00-2P | 850249-01-3P | 850249-02-4P |

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| 850249-92-2P | | | | |

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino-substituted pyrimidines as antitumor agents)

L110 ANSWER 19 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:735326 HCAPLUS Full-text

DOCUMENT NUMBER: 143:229730

TITLE: Preparation of tetrahydroisoquinoline derivatives for treating diseases mediated by protein trafficking or chloride channel activity

INVENTOR(S): Pregel, Marko J.; Hirth, Bradford H.; Kane, John L.; Qiao, Shuang; Gregory, Jill; Cuff, Lisa

PATENT ASSIGNEE(S): Genzyme Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 52 pp.

CODEN: USXXCO

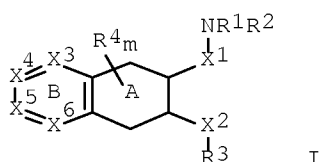
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|--|-----------------|----------------|
| ----- | ---- | ----- | ----- | ----- |
| US 20050176761 | A1 | 20050811 | US 2004-6042 | 20041207 <-- |
| PRIORITY APPLN. INFO.: | | | US 2003-531873P | P 20031223 <-- |
| OTHER SOURCE(S): | | CASREACT 143:229730; MARPAT 143:229730 | | |
| GI | | | | |



AB Tetrahydroisoquinoline derivs. I (variables defined below), pharmaceutical compns. comprising them and methods of treating disease are disclosed herein.

The disclosed compds. are useful in the treatment and prevention of diseases mediated by chloride channel activity and/or protein trafficking, including, but not limited to, diseases associated with impaired mucociliary clearance such as cystic fibrosis, bronchitis, emphysema, and the like. For I the variables are: X1 = CH₂, CO, SO, SO₂; X2 = CH₂, CO, COCH₂, CO₂, COS, O, S, SO; X3, X4, X5, X6 = N, CH, wherein at least 1 of X3, X4, X5, X6 = CH; Ring B is optionally substituted in any substitutable carbon; R1 and R2 = H or an optionally substituted aliphatic, aryl, heteroaryl, heterocyclic, cycloalkyl, peptide, or amino acid group, provided that R1 and R2 are not both H; or, R1 and R2, taken together with the nitrogen to which they are bonded, are an optionally substituted heterocyclic group; R3 = optionally substituted aryl, heteroaryl, cycloalkyl, or heterocyclic group; m = 0-2; each R4 = halogen, OH, SH, Ra, ORa, SRa, NH₂, NHRa, NRa₂, C(O)NRa₂, CF₃, CN, or NO₂; and Ra = C1-C5 branched or linear alkyl group.

IT 851777-89-4F

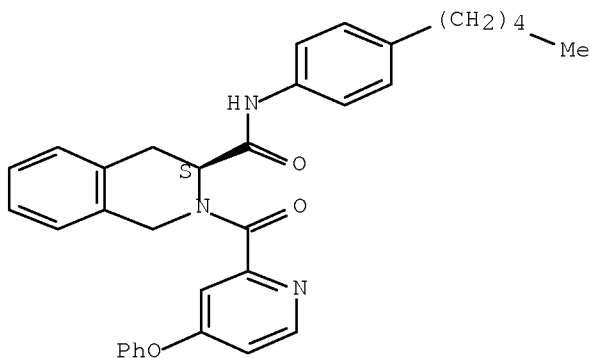
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of tetrahydroisoquinoline derivs. for treating diseases mediated by protein trafficking or chloride channel activity)

RN 851777-89-4 HCAPLUS

CN 3-Isoquinolinecarboxamide, 1,2,3,4-tetrahydro-N-(4-pentylphenyl)-2-[(4-phenoxy-2-pyridinyl)carbonyl]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-4709

ICS A61K031-47

INCL 514310000

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT 851777-43-0P 851777-46-3P 851777-47-4P 851777-48-5P 851777-49-6P
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 2-(3-Phenoxybenzoyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid
 N-(4-heptylphenyl)amide 851777-55-4P 851777-56-5P 851777-57-6P
 851777-59-8P 851777-60-1P 851777-61-2P 851777-62-3P 851777-63-4P,
 (S)-2-(3-Phenoxybenzoyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid
 N-(6-pentylpyridin-3-yl)amide 851777-64-5P 851777-66-7P 851777-67-8P
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 851777-77-0P 851777-79-2P 851777-80-5P 851777-81-6P 851777-83-8P
 851777-84-9P 851777-85-0P 851777-86-1P 851777-89-4F
 851777-90-7P 851777-91-8P 851777-92-9P 851777-93-0P,
 (S)-2-[[5-(Cyclohexyloxy)pyridin-3-yl]carbonyl]-1,2,3,4-

tetrahydroisoquinoline-3-carboxylic acid N-(4-pentylphenyl)amide
 851777-94-1P 851777-95-2P, (S)-2-(2-Isopropoxy-pyridine-4-carbonyl)-
 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (4-pentylphenyl)amide
 862504-12-9P 862504-13-0P 862504-14-1P 862504-15-2P 862504-16-3P
 862504-17-4P 862504-18-5P 862504-19-6P 862504-20-9P 862504-21-0P
 862504-22-1P 862504-23-2P 862504-24-3P, 2-[(Naphthalen-2-yl)carbonyl]-
 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid N-(4-chlorophenyl)amide
 862504-25-4P 862504-26-5P 862504-27-6P 862504-28-7P 862504-29-8P
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 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(drug candidate; preparation of tetrahydroisoquinoline derivs. for treating
 diseases mediated by protein trafficking or chloride channel activity)

L110 ANSWER 20 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:641861 HCAPLUS Full-text

DOCUMENT NUMBER: 143:146651

TITLE: JAK/STAT inhibitors and MAPK/ERK inhibitors for
 respiratory syncytial virus (RSV) infection

INVENTOR(S): Mohapatra, Shyam S.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 46 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------------|
| US 20050159385 | A1 | 20050721 | US 2004-18954 | 20041220 <-- |
| PRIORITY APPLN. INFO.: | | | US 2003-531052P | P 20031219 <-- |

AB The invention discloses a method for treating or reducing the likelihood of
 developing a RSV infection in a subject by administering an effective amount

10/590724

of an inhibitor of the janus kinase (JAK)/signal transducer and activator of transcription (STAT) signaling pathway or the mitogen-activated kinase (MAPK)/extracellular signal-regulated kinase (ERK1/2) signaling pathway to the subject. Also disclosed is a pharmaceutical composition that includes an inhibitor of JAK/STAT or MAPK/ERK signaling to the subject; and a pharmaceutically acceptable carrier. Further disclosed is a method for identifying agents useful for treating or reducing the likelihood of developing an RSV infection.

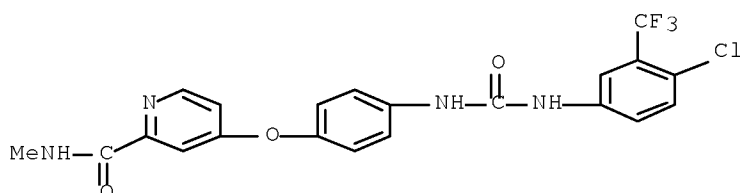
IT 284461-73-0, BAY 43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(JAK/STAT inhibitors and MAPK/ERK inhibitors for respiratory syncytial virus infection treatment)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K048-00

ICS A61K039-395; A61K038-17

INCL 514044000; 514002000; 424146100

CC 1-5 (Pharmacology)

IT 4959-60-8, 4,5-Dimethoxy-2-nitrobenzamide 4998-07-6,
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66575-29-9, Forskolin 109511-58-2, U0126 133550-30-8, AG490
167869-21-8, PD98059 177075-18-2, ISIS 5132 201653-76-1 202475-60-3,
4-4'-Hydroxyphenylamino-6,7-dimethoxyquinazoline 210419-07-1, Ro 09-2210
211555-04-3 212631-79-3, PD184352 220904-83-6, GW5074
284461-73-0, BAY 43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(JAK/STAT inhibitors and MAPK/ERK inhibitors for respiratory syncytial virus infection treatment)

L110 ANSWER 21 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:469894 HCAPLUS Full-text

DOCUMENT NUMBER: 143:7592

TITLE: Preparation of arylpyrrolecarboxamides as Raf kinase inhibitors for treatment of tumors.

INVENTOR(S): Finsinger, Dirk; Buchstaller, Hans-Peter; Burgdorf, Lars; Wiesner, Matthias; Amendt, Christiane; Grell, Matthias; Sirrenberg, Christian; Zenke, Frank

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: Ger. Offen., 32 pp.
CODEN: GWXXBX

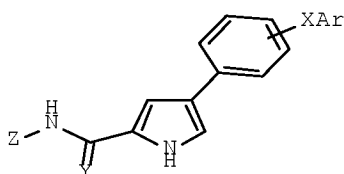
DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-----------------|------------------|----------------|
| DE 10354060 | A1 | 20050602 | DE 2003-10354060 | 20031119 <-- |
| AU 2004291255 | A1 | 20050602 | AU 2004-291255 | 20041026 <-- |
| CA 2546334 | A1 | 20050602 | CA 2004-2546334 | 20041026 <-- |
| WO 2005049603 | A1 | 20050602 | WO 2004-EP12076 | 20041026 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1685125 | A1 | 20060802 | EP 2004-790859 | 20041026 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| CN 1882571 | A | 20061220 | CN 2004-80034345 | 20041026 <-- |
| BR 2004016690 | A | 20070130 | BR 2004-16690 | 20041026 <-- |
| JP 2007511553 | T | 20070510 | JP 2006-540216 | 20041026 <-- |
| IN 2006KN00936 | A | 20070420 | IN 2006-KN936 | 20060417 <-- |
| MX 2006PA05478 | A | 20060811 | MX 2006-PA5478 | 20060515 <-- |
| US 20070149594 | A1 | 20070628 | US 2006-579825 | 20060517 <-- |
| PRIORITY APPLN. INFO.: | | | DE 2003-10354060 | A 20031119 <-- |
| | | | WO 2004-EP12076 | W 20041026 |
| OTHER SOURCE(S): | | MARPAT 143:7592 | | |
| GI | | | | |



I

AB Title compds. [I; Ar = (substituted) Ph, naphthyl, biphenyl, heterocyclyl; X = O, S, (CH₂)_n, CO, (CH₂)_nO, (CH₂)_nNH, etc.; n = 1-3; Y = O, S, CHNO₂, C(CN)₂, NR₄; R₄ = H, cyano, OH, etc.; Z = Ar, ArXAr, CH₂Ar, CH₂ArXAr; Ar = (substituted) Ph], were prepared as Raf kinase inhibitors (no data). Thus, 4-(PhCH₂O)C₆H₄CH₂CO₂H, DMF, and POCl₃ were heated together at 70° for 4 h followed by cooling and addition of ice water and aqueous NaClO₄ to give 98% [2-(4-benzyloxyphenyl)-3-dimethylaminoallylidene]dimethylammonium perchlorate. This was refluxed 24 h with glycine Et ester hydrochloride in EtOH containing 20% NaOEt to give 91% Et 4-(4-benzyloxyphenyl)-1H-pyrrole-2- carboxylate. Hydrogenolysis of the latter in EtOAc over Pd/C gave 91% Et 4-(4-hydroxyphenyl)-1H-pyrrole-2-carboxylate. This was heated with 4-chloropyridine-2-carboxylic acid N-methylamide at 160° for 48 h to give 40% Et 4-[4-(2-methylcarbamoylpyridin-4-yloxy)phenyl]-1H-pyrrole-2- carboxylate. Saponification with 2N NaOH in EtOH at 60° for 16 h followed by acidification

with HCl gave 85% free acid, which was stirred 48 h in DMF with 5-amino-2-chlorobenzotrifluoride, N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride, and 1-hydroxybenzotriazole hydrate to give 17% 4-[4-[5-(4-chloro-3-trifluoromethylphenyl)carbamoyl]-1H-pyrrol-3-yl]phenoxy]pyridine-2-carboxylic acid N-methylamide.

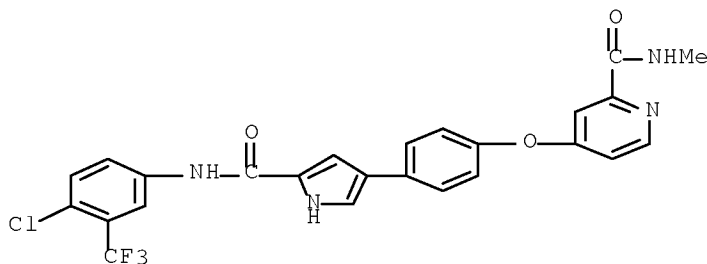
IT 852455-19-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of arylpyrrolecarboxamides as Raf kinase inhibitors for treatment of tumors)

RN 852455-19-7 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]-1H-pyrrol-3-yl]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D401-12

ICS A61K031-4439; A61P035-00; A61P017-00; A61P019-00; A61P031-00; A61P013-00; A61P037-00

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT 852455-19-7P 852455-20-0P 852455-21-1P
852455-22-2P 852455-23-3P 852455-24-4P
852455-25-5P 852455-26-6P 852455-27-7P
852455-28-8P 852455-29-9P 852455-30-2P
852455-31-3P 852455-32-4P 852455-33-5P
852455-34-6P 852455-35-7P 852455-36-8P
852455-37-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of arylpyrrolecarboxamides as Raf kinase inhibitors for treatment of tumors)

L110 ANSWER 22 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:1154653 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 142:93545

TITLE: Preparation of diaryl ureas with kinase inhibiting activity

INVENTOR(S): Wilhelm, Scott; Dumas, Jacques; Ladouceur, Gaetan; Lynch, Mark; Scott, William J.

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 122 pp.

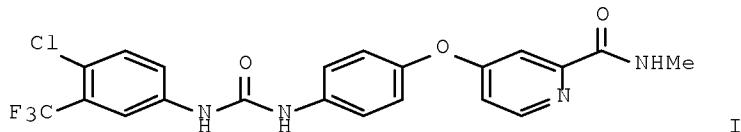
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------------|
| ----- | ---- | ----- | ----- | ----- |
| WO 2004113274 | A2 | 20041229 | WO 2004-US15655 | 20040519 <-- |
| WO 2004113274 | A3 | 20050303 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2526617 | A1 | 20041229 | CA 2004-2526617 | 20040519 <-- |
| US 20050059703 | A1 | 20050317 | US 2004-848567 | 20040519 <-- |
| EP 1636585 | A2 | 20060322 | EP 2004-752642 | 20040519 <-- |
| EP 1636585 | B1 | 20080116 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| JP 2007511203 | T | 20070510 | JP 2006-533211 | 20040519 <-- |
| AT 366108 | T | 20070715 | AT 2004-776037 | 20040519 <-- |
| ES 2288694 | T3 | 20080116 | ES 2004-776037 | 20040519 <-- |
| AT 384264 | T | 20080215 | AT 2004-752642 | 20040519 <-- |
| MX 2005PA12491 | A | 20060929 | MX 2005-PA12491 | 20051118 <-- |
| US 20070020704 | A1 | 20070125 | US 2006-571100 | 20060728 <-- |
| PRIORITY APPLN. INFO.: | | | US 2003-471735P | P 20030520 <-- |
| | | | US 2003-520399P | P 20031117 <-- |
| | | | US 2004-556062P | P 20040325 |
| | | | WO 2004-US15655 | W 20040519 |
| OTHER SOURCE(S): MARPAT 142:93545 | | | | |
| GI | | | | |



AB Diaryl ureas B-NH-CO-NH-L-(CH₂)_m-X-(CH₂)_p-L₁-(Q)₁₋₃ [I; B = (un)substituted Ph, naphthyl, or heteroaryl; L, = (un)substituted Ph, naphthyl, or heteroaryl; X = bond, O, CO, NR₃, NR₃CO, S, CONR₃, CF₂, CC1₂, CHF, CH(OH), C.tplbond.C, CH:CH, CR₄R₅; m, p = independently 0-4; L₁ = any group L, 5-6 membered cyclic structure; Q = independently COR₄, CO₂R₄, CONR₄R₅; each R₃-R₅ = independently H, (un)substituted C1-5 alkyl, C3-5 cycloalkyl, Ph, C1-3 alkylphenyl, C0-4 alkylheteroaryl], useful to treat diseases and conditions associated with signal transduction pathways comprising of at least one of raf, VEGFR, PDGFR, p38 and/or FLT-3. E.g., a multi-step synthesis of the urea II which produced dose-dependent 45-68% inhibition of tumor growth in a staged HCT 116 colon (mutant k-Ras) xenograft model.

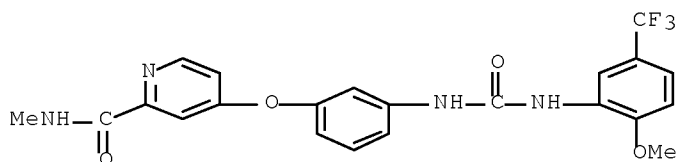
IT 284461-42-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diaryl ureas with kinase inhibiting activity)

RN 284461-42-3 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07C273-18

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 63

IT 228418-48-2P 284461-33-2P 284461-34-3P 284461-35-4P 284461-36-5P
284461-37-6P 284461-38-7P 284461-39-8P 284461-40-1P 284461-41-2P
284461-42-3P 284461-43-4P 284461-44-5P
284461-45-6P 284461-46-7P 284461-47-8P
284461-48-9P 284461-49-0P 284461-50-3P
284461-51-4P 284461-52-5P 284461-53-6P 284461-54-7P
284461-55-8P 284461-56-9P 284461-57-0P 284461-58-1P
284461-59-2P 284461-60-5P 284461-61-6P 284461-62-7P
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284461-68-3P 284461-69-4P 284461-70-7P 284461-71-8P 284461-72-9P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diaryl ureas with kinase inhibiting activity)

L110 ANSWER 23 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:965067 HCAPLUS Full-text

DOCUMENT NUMBER: 141:406039

TITLE: Combinations for the treatment of diseases involving cell proliferation, migration or apoptosis of myeloma

10/590724

cells, or angiogenesis

INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin
Friedrich; Baum, Anke; Munzert, Gerd; Van Meel,
Jacobus C. A.

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany;
Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.

SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------------|
| WO 2004096224 | A2 | 20041111 | WO 2004-EP4363 | 20040424 <-- |
| WO 2004096224 | A3 | 20041216 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1473043 | A1 | 20041103 | EP 2003-9587 | 20030429 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| AU 2004233576 | A1 | 20041111 | AU 2004-233576 | 20040424 <-- |
| CA 2523868 | A1 | 20041111 | CA 2004-2523868 | 20040424 <-- |
| EP 1622619 | A2 | 20060208 | EP 2004-729366 | 20040424 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| BR 2004009919 | A | 20060425 | BR 2004-9919 | 20040424 <-- |
| JP 2006524634 | T | 20061102 | JP 2006-500099 | 20040424 <-- |
| MX 2005PA11656 | A | 20051215 | MX 2005-PA11656 | 20051028 <-- |
| NO 2005005605 | A | 20051128 | NO 2005-5605 | 20051128 <-- |
| PRIORITY APPLN. INFO.: | | | EP 2003-9587 | A 20030429 <-- |
| | | | EP 2004-508 | A 20040113 |
| | | | EP 2004-1171 | A 20040121 |
| | | | WO 2004-EP4363 | W 20040424 |

AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination preps. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

IT 284461-73-0, BAY-43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

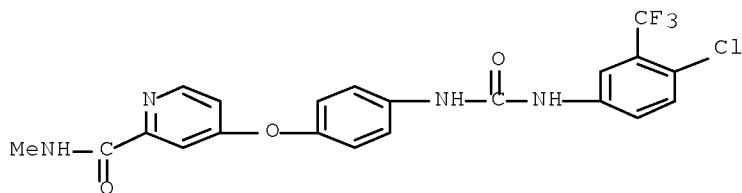
(drug combinations for diseases involving cell proliferation and migration or apoptosis or angiogenesis including protein tyrosine

10/590724

kinase receptor antagonists and radiotherapy)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c
arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K031-496

ICS A61K031-517; A61P035-00

CC 1-6 (Pharmacology)

Section cross-reference(s): 8, 15

IT 183321-74-6, Erlotinib 183552-38-7, Abarelix 184475-35-2, Gefitinib
185243-69-0, Etanercept 187724-61-4, PKI-166 190977-41-4, Oblimersen
191732-72-6, Revimid 204005-46-9, SU-5416 205923-56-4, Cetuximab
206181-63-7, Ibritumomab 212141-54-3, Vatalanib 213327-37-8,
Oregovomab 215369-21-4, DC 101 216503-57-0, Alemtuzumab 216503-58-1,
Mitumomab 216974-75-3, Avastin 252003-65-9, CP-547632 252916-29-3,
SU-6668 257933-82-7, EKB-569 262367-70-4 263338-11-0 267227-08-7,
Apolizumab 284461-73-0, BAY-43-9006 288383-20-0 289499-45-2,
CI-1033 305838-77-1, Neovastat 319460-85-0 334949-28-9 334949-30-3
334949-31-4 334949-32-5 334949-38-1 334950-47-9 339186-68-4,
EMD-72000 402857-58-3, CEP-7055 437755-78-7, GW 2016 439081-18-2
439943-59-6, TLK-286 443913-73-3 444731-52-6, GW 786034 543726-73-4,
IMC 1C11 591207-53-3, LAQ 824 656247-17-5 660412-20-4 660412-24-8
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275 (pharmaceutical) 790713-30-3, BAY 57-9006 790713-36-9, IM 842
790713-55-2, AZD 6474 790713-57-4, BMY 42355 791073-97-7, 1D09C3
892553-42-3, Vitaxin

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(drug combinations for diseases involving cell proliferation and
migration or apoptosis or angiogenesis including protein tyrosine
kinase receptor antagonists and radiotherapy)

L110 ANSWER 24 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:817864 HCAPLUS Full-text

DOCUMENT NUMBER: 141:314164

TITLE: preparation of pyridinyloxyphenylethanediarnide derivs. as
RAF-kinase inhibitors

INVENTOR(S): Buchstaller, Hans-Peter; Wiesner, Matthias; Zenke,
Frank; Amendt, Christiane; Grell, Matthias;
Sirrenberg, Christian

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 197 pp.

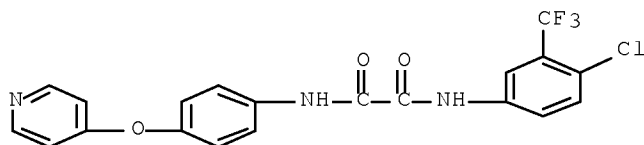
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|------------------|----------------|
| WO 2004085399 | A1 | 20041007 | WO 2004-EP2406 | 20040309 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004224239 | A1 | 20041007 | AU 2004-224239 | 20040309 <-- |
| CA 2520009 | A1 | 20041007 | CA 2004-2520009 | 20040309 <-- |
| EP 1606260 | A1 | 20051221 | EP 2004-718645 | 20040309 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | | |
| BR 2004007968 | A | 20060307 | BR 2004-7968 | 20040309 <-- |
| CN 1764645 | A | 20060426 | CN 2004-80007867 | 20040309 <-- |
| JP 2006521304 | T | 20060921 | JP 2006-504603 | 20040309 <-- |
| US 20060189665 | A1 | 20060824 | US 2005-549852 | 20050923 <-- |
| PRIORITY APPLN. INFO.: | | | EP 2003-6702 | A 20030324 <-- |
| | | | WO 2004-EP2406 | W 20040309 |
| OTHER SOURCE(S): CASREACT 141:314164; MARPAT 141:314164 | | | | |
| AB ADB [D = (substituted) bivalent oxamide moiety; A = L(ML1)a; L = 5-7 membered cyclic structure, preferably aryl, heteroaryl, arylene, heteroarylene; L1 = (substituted) cyclic moiety having at least 5 members, preferably aryl, heteroaryl, aralkyl, cycloalkyl, heterocyclyl; M = bond, bridging group; a = 1-4; L, L1 contain 0-4 N, O, S atoms; B = (substituted) up to tricyclic aryl, heteroaryl containing 0-4 N, O, S atoms], were prepared for treatment of hyperproliferative and nonhyperproliferative disorders (no data). For example, reaction of N-(4-chloro-3- trifluoromethylphenyl)-2-oxoglycine (preparation given) with 4-(4-pyridinyloxy)phenylamine yielded N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-(4-pyridinyloxy)phenyl]ethanediamine. | | | | |
| IT 767358-34-9P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of pyridinyloxyphenylethanediame derivs. as RAF-kinase inhibitors) | | | | |
| RN 767358-34-9 HCAPLUS | | | | |
| CN Ethanediamide, N1-[4-chloro-3-(trifluoromethyl)phenyl]-N2-[4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME) | | | | |



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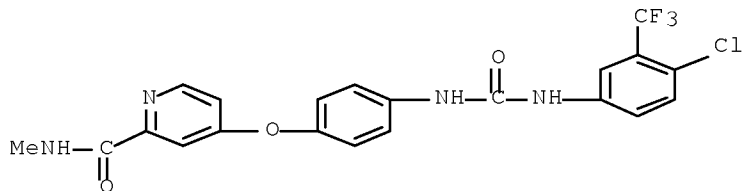
ICS C07D413-12; C07D213-81; A61P031-00; A61K031-4427; A61P017-06
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
IT 767358-34-9P 767358-35-0P 767358-36-1P 767358-37-2P
767358-38-3P 767358-39-4P 767358-40-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of pyridinyloxyphenylethanedi-
amides as RAF-kinase inhibitors)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 25 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:802884 HCAPLUS Full-text
DOCUMENT NUMBER: 141:289056
TITLE: Medical use of ras antagonists for the treatment of
capillary malformation
INVENTOR(S): Vikkula, Miikka; Boon, Laurence; Eerola, Iiro
PATENT ASSIGNEE(S): Universite Catholique De Louvain, Belg.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|----------------|
| WO 2004083458 | A1 | 20040930 | WO 2003-EP2913 | 20030320 <-- |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2515519 | A1 | 20040930 | CA 2003-2515519 | 20030320 <-- |
| AU 2003214145 | A1 | 20041011 | AU 2003-214145 | 20030320 <-- |
| EP 1604037 | A1 | 20051214 | EP 2003-709806 | 20030320 <-- |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| US 20060141472 | A1 | 20060629 | US 2005-546692 | 20050928 <-- |
| PRIORITY APPLN. INFO.: | | | WO 2003-EP2913 | W 20030320 <-- |
| AB | The invention relates to the field of vascular anomalies and methods for diagnosing and treating them. The invention provides for the causative gene (RASA1) and mutations therein which are useful for diagnosing inherited capillary malformations. The invention further provides RASA1 antagonists for use in treatment of capillary malformations. | | | |
| IT | 284461-73-0, BAY 43-9006 | | | |
| RL: | PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (Raf protein inhibitor; diagnosis and treatment of vascular anomalies using primers to detect RASA1 gene mutations and ras protein antagonists) | | | |
| RN | 284461-73-0 HCAPLUS | | | |
| CN | 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c | | | |

10/590724

carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C12Q001-68
ICS A61K031-00
CC 1-8 (Pharmacology)
Section cross-reference(s): 3
IT 177075-18-2, ISIS 5132 284461-73-0, BAY 43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(Raf protein inhibitor; diagnosis and treatment of vascular anomalies
using primers to detect RAS1 gene mutations and ras protein
antagonists)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 26 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:756710 HCAPLUS Full-text
DOCUMENT NUMBER: 141:277628
TITLE: Preparation of ureidophenoxycyanopyridines as
anticancer drugs.
INVENTOR(S): Scott, William J.; Dumas, Jacques; Boyer, Stephen;
Lee, Wendy; Chen, Yuanwei; Phillips, Barton; Verma,
Sharad; Chen, Jianqing; Chen, Zhi; Fan, Jianmei;
Raudenbush, Brian; Redman, Aniko; Yi, Lin; Zhu,
Qingming
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| WO 2004078747 | A1 | 20040916 | WO 2004-US6286 | 20040301 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 20040235829 | A1 | 20041125 | US 2004-788029 | 20040227 <-- |
| AU 2004217977 | A1 | 20040916 | AU 2004-217977 | 20040301 <-- |
| CA 2517361 | A1 | 20040916 | CA 2004-2517361 | 20040301 <-- |

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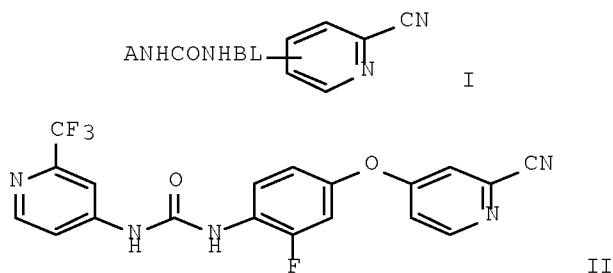
| | | | | |
|----------------|----|----------|----------------|--------------|
| US 20040229937 | A1 | 20041118 | US 2004-789446 | 20040301 <-- |
| US 20050032798 | A1 | 20050210 | US 2004-788405 | 20040301 <-- |
| US 20050038031 | A1 | 20050217 | US 2004-788426 | 20040301 <-- |
| EP 1599467 | A1 | 20051130 | EP 2004-716144 | 20040301 <-- |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK

| | | | | |
|----------------|---|----------|------------------|--------------|
| BR 2004007897 | A | 20060301 | BR 2004-7897 | 20040301 <-- |
| JP 2006519264 | T | 20060824 | JP 2006-508977 | 20040301 <-- |
| CN 1839126 | A | 20060927 | CN 2004-80011547 | 20040301 <-- |
| IN 2005DN03802 | A | 20070824 | IN 2005-DN3802 | 20050826 <-- |

PRIORITY APPLN. INFO.: US 2003-450323P P 20030228 <--
US 2003-450324P P 20030228 <--
US 2003-450348P P 20030228 <--
WO 2004-US6286 A 20040301

OTHER SOURCE(S): CASREACT 141:277628; MARPAT 141:277628
GI

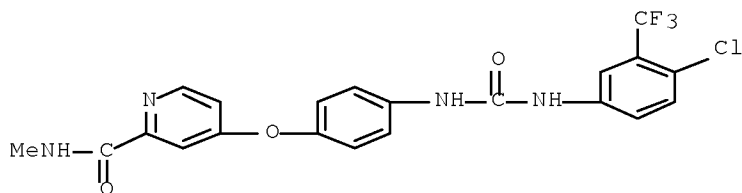


AB Title compds. [I; A = (substituted) pyridinyl, naphthyl, 8-10 membered bicyclic heteroaryl, heterocyclyl, carbocyclyl; B = (substituted) phenylene, naphthylenediyl; L = O, S; m = 0-3; R2 = alkyl, haloalkyl, alkoxy, N-oxo, N-hydroxy], were prepared Thus, 2-trifluoromethyl-4- pyridylamine was stirred 20 h with carbonyldiimidazole in CH₂Cl₂; 4-(4-amino-3-fluorophenoxy)pyridine-2-carbonitrile (preparation given) was added followed by stirring for 1 day to give 75% title compound (II). I inhibited c-RAF-1 kinase with IC₅₀ = 7.86 nM to >1600 nM.

IT 284461-73-0, Bay 43-9006
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of ureidophenoxycyanopyridines as anticancer drugs)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D401-12
 ICS C07D405-12; C07D213-79; C07D417-12; A61K031-443; A61K031-444;
 A61K031-4433; A61K031-4436; A61P035-00

CC 28-11 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1, 27, 63

IT 184475-35-2, Iressa 190977-41-4, Oblimersen 191732-72-6, CDC 501
 192185-72-1, Tipifarnib 193275-84-2, Lonaferon 195533-53-0, T-138067
 196488-72-9, Ranpirnase 198153-51-4, Pegasys 199396-76-4, Asoprisnil
 199796-52-6, Taxoprexin 205923-56-4, Cetuximab 206181-63-7,
 Ibiritumomab tiuxetan 208265-92-3, Neulasta 208921-02-2, Tositumomab
 209810-58-2, Aranesp 212141-54-3, Vatalanib 215647-85-1, PEG-intron
 216503-57-0, Campath 216586-46-8, Virulizin 216974-75-3, Avastin
 219989-84-1, Ixabepilone 220127-57-1, Gleevec 220578-59-6, Gemtuzumab
 ozogamicin 220581-49-7, Rebif 223378-40-3, Alferon N 263351-82-2,
 CT-2103 284461-73-0, Bay 43-9006 305838-77-1, Neovastat
 416841-63-9, Alfaferone 439943-59-6, Tlk-286 606967-38-8, MX 6
 646032-04-4, R 1549 675625-06-6, Affinitak

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (coadministration; preparation of ureidophenoxycyanopyridines as anticancer
 drugs)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 27 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:754414 HCAPLUS Full-text

DOCUMENT NUMBER: 141:277492

TITLE: Preparation of pyridine-containing diaryl ureas useful
 in the treatment of cancer and other disorders

INVENTOR(S): Dumas, Jacques; Lee, Wendy; Chen, Yuanwei; Adnane,
 Lila; Scott, William J.; Verma, Sharad; Chen,
 Jianging; Chen, Zhi; Yi, Lin

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 96 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

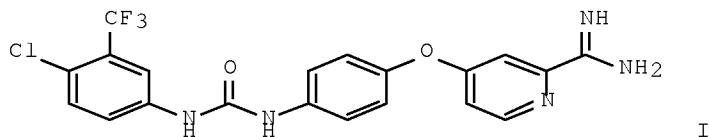
FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|----------------|
| WO 2004078128 | A2 | 20040916 | WO 2004-US6295 | 20040301 <-- |
| WO 2004078128 | A3 | 20041223 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2516627 | A1 | 20040916 | CA 2004-2516627 | 20040301 <-- |
| EP 1603879 | A2 | 20051214 | EP 2004-716142 | 20040301 <-- |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | |
| JP 2006519266 | T | 20060824 | JP 2006-508981 | 20040301 <-- |
| MX 2005PA09102 | A | 20060531 | MX 2005-PA9102 | 20050826 <-- |
| PRIORITY APPLN. INFO.: | | | US 2003-450324P | P 20030228 <-- |
| | | | WO 2004-US6295 | W 20040301 |

10/590724

OTHER SOURCE(S): MARPAT 141:277492
GI



AB The title novel pyridine-containing diaryl ureas ANHC(O)NHBLMQ [A = (un)substituted Ph, naphthyl, heteroaryl, etc.; B = (un)substituted Ph, naphthyl, pyridyl; L = (CH₂)_mO(CH₂)_l, (CH₂)_m(CH₂)_l, (CH₂)_mC(O)(CH₂)_l, etc.; m, l = 0-4; M = (un)substituted pyridine; Q = tetrazolyl, imidazolyl, thiazolinyl, etc.], useful for treating hyper-proliferative and angiogenesis disorders, as a sole agent or in combination with cytotoxic therapies, were prepared and formulated. E.g., a multi-step synthesis of I, was given.

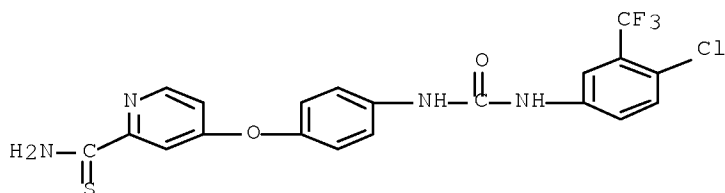
IT 758709-43-2P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of pyridine-containing diaryl ureas for treating cancer and other disorders)

RN 758709-43-2 HCAPLUS

CN 2-Pyridinecarbothioamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (CA INDEX NAME)



IC ICM A61K

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

IT 758709-43-2P 758709-45-4P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of pyridine-containing diaryl ureas for treating cancer and other disorders)

IT 758709-37-4P 758709-38-5P 758709-40-9P 758709-41-0P
758709-47-6P 758709-49-8P 758709-51-2P 758709-53-4P
758709-55-6P 758709-57-8P 758709-59-0P 758709-61-4P
758709-63-6P 758709-65-8P 758709-67-0P
758709-69-2P 758709-71-6P 758709-73-8P

758709-75-0P 758709-77-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of pyridine-containing diaryl ureas for treating cancer and
other disorders)

IT 24484-93-3P 51727-15-2P 73771-11-6P 220000-87-3P
228400-44-0P 284462-37-9P 284462-78-8P 573673-43-5P
630125-69-8P 757229-80-4P 757230-16-3P 757249-68-6P 757250-67-2P
757251-59-5P 757251-60-8P 757251-79-9P 758709-84-1P 758709-88-5P
758709-89-6P 758709-90-9P 758709-91-0P 758709-92-1P
758709-93-2P 758709-94-3P 758709-95-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of pyridine-containing diaryl ureas for treating cancer and
other disorders)

L110 ANSWER 28 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:428911 HCAPLUS Full-text

DOCUMENT NUMBER: 141:7028

TITLE: Preparation of 3-substituted-6-aryl pyridines ligands
of C5a receptors

INVENTOR(S): Hutchison, Alan; Yuan, Jun; Lee, Kyungae; Maynard,
George; Chenard, Bertrand L.; Liu, Nian; Guo, Qin;
Guo, Zihong; Hrnciar, Peter

PATENT ASSIGNEE(S): Neurogen Corporation, USA

SOURCE: PCT Int. Appl., 366 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

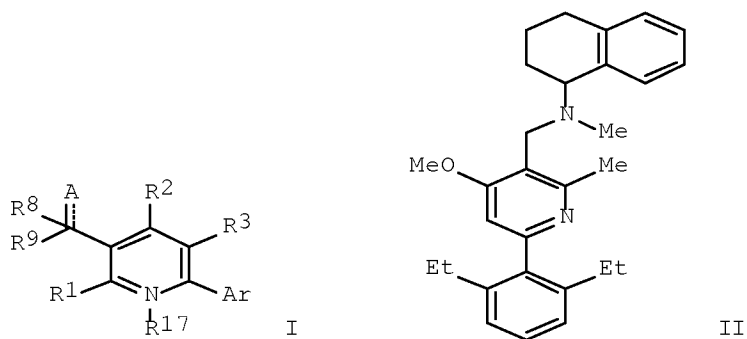
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|----------------|
| WO 2004043925 | A2 | 20040527 | WO 2003-US35694 | 20031107 <-- |
| WO 2004043925 | A3 | 20040805 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2504941 | A1 | 20040527 | CA 2003-2504941 | 20031107 <-- |
| AU 2003291403 | A1 | 20040603 | AU 2003-291403 | 20031107 <-- |
| US 20040158067 | A1 | 20040812 | US 2003-704364 | 20031107 <-- |
| US 7342115 | B2 | 20080311 | | |
| EP 1565452 | A2 | 20050824 | EP 2003-768799 | 20031107 <-- |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| PRIORITY APPLN. INFO.: | | | US 2002-425281P | P 20021108 <-- |
| | | | WO 2003-US35694 | W 20031107 <-- |

OTHER SOURCE(S): MARPAT 141:7028

GI



AB The title compds. [I; Ar = (un)substituted Ph, naphthyl, pyridyl, etc.; A = OR₄, NR₄R₅, CR₆R₇, CHR₆R₇; R₁ = H, halo, NH₂, CN, etc.; R₂ = halo, CN, XR; R₃ = H, halo, OH, etc.; R₄ = alkyl, alkenyl, benzoisothiazolyl, etc.; R₅ = H, alkyl, alkenyl, etc.; R₆ = halo, OH, CN, etc.; R₇ = H, halo, OH, etc.; R₈ = H, halo, OH, etc.; R₉ = absent, H, halo, OH, etc.; X = a bond, O, CO, etc.; R = H, alkyl, alkenyl, etc.; R₁₇ = absent, O] which bind to C₅a receptors with high affinity and exhibit neutral antagonist or inverse agonist activity at C₅a receptors, and therefore are useful in treating a variety of inflammatory, cardiovascular, and immune system disorders, were prepared and formulated. E.g., a multi-step synthesis of II is given. In addition, the present invention provides labeled 3-substituted-6-aryl pyridines I, which are useful as probes for the localization of C₅a receptors.

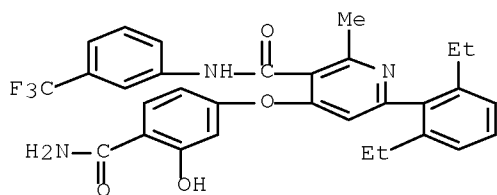
IT 693277-81-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 3-substituted-6-aryl pyridines as ligands of C₅a receptors)

RN 693277-81-5 HCAPLUS

CN 3-Pyridinecarboxamide, 4-[4-(aminocarbonyl)-3-hydroxyphenoxy]-6-(2,6-diethylphenyl)-2-methyl-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



IC ICM C07D213-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 63

| | | | | | |
|----|--------------|--------------|--------------|--------------|--------------|
| IT | 693276-88-9P | 693276-89-0P | 693276-90-3P | 693276-91-4P | 693276-92-5P |
| | 693276-93-6P | 693276-94-7P | 693276-95-8P | 693276-96-9P | 693276-97-0P |
| | 693276-98-1P | 693276-99-2P | 693277-00-8P | 693277-01-9P | 693277-02-0P |

| | | | | |
|--------------|--------------|--------------|--------------|--------------|
| 693277-03-1P | 693277-04-2P | 693277-05-3P | 693277-06-4P | 693277-07-5P |
| 693277-08-6P | 693277-09-7P | 693277-10-0P | 693277-11-1P | 693277-12-2P |
| 693277-13-3P | 693277-14-4P | 693277-15-5P | 693277-16-6P | 693277-17-7P |
| 693277-18-8P | 693277-19-9P | 693277-20-2P | 693277-21-3P | 693277-22-4P |
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| 693277-58-6P | 693277-59-7P | 693277-60-0P | 693277-61-1P | 693277-62-2P |
| 693277-63-3P | 693277-64-4P | 693277-65-5P | 693277-66-6P | 693277-67-7P |
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| 693277-82-6P | 693277-83-7P | 693277-84-8P | 693277-85-9P | 693277-86-0P |
| 693277-87-1P | 693277-88-2P | 693277-89-3P | 693277-90-6P | 693277-91-7P |
| 693277-92-8P | 693277-93-9P | 693277-94-0P | 693277-95-1P | 693277-96-2P |
| 693277-97-3P | 693277-98-4P | 693277-99-5P | 693278-00-1P | 693278-01-2P |
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| 693278-93-2P | 693278-94-3P | 693278-95-4P | 693278-96-5P | 693278-97-6P |
| 693278-98-7P | 693278-99-8P | 693279-00-4P | 693279-01-5P | 693279-02-6P |
| 693279-03-7P | 693279-04-8P | 693279-05-9P | 693279-06-0P | 693279-07-1P |
| 693279-08-2P | 693279-09-3P | 693279-11-7P | 693279-13-9P | 693279-14-0P |
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of 3-substituted-6-aryl pyridines as ligands of C5a receptors)

L110 ANSWER 29 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:370904 HCAPLUS Full-text

DOCUMENT NUMBER: 140:391200

TITLE: Preparation of pyridinyloxybenzylureas as RAF kinase inhibitors.

INVENTOR(S): Buchstaller, Hans-Peter; Wiesner, Matthias; Schadt, Oliver; Amendt, Christiane; Zenke, Frank; Sirrenberg, Christian; Grell, Matthias; Finsinger, Dirk

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 341 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|------------------|----------------|
| WO 2004037789 | A2 | 20040506 | WO 2003-EP11134 | 20031008 <-- |
| WO 2004037789 | A3 | 20041028 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2503445 | A1 | 20040506 | CA 2003-2503445 | 20031008 <-- |
| AU 2003268926 | A1 | 20040513 | AU 2003-268926 | 20031008 <-- |
| EP 1562905 | A2 | 20050817 | EP 2003-750697 | 20031008 <-- |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| BR 2003015580 | A | 20050830 | BR 2003-15580 | 20031008 <-- |
| CN 1705645 | A | 20051207 | CN 2003-80101925 | 20031008 <-- |
| JP 2006506454 | T | 20060223 | JP 2005-501513 | 20031008 <-- |
| MX 2005PA04206 | A | 20050608 | MX 2005-PA4206 | 20050420 <-- |
| US 20060199844 | A1 | 20060907 | US 2005-532574 | 20050425 <-- |
| ZA 2005004175 | A | 20060329 | ZA 2005-4175 | 20060117 <-- |
| PRIORITY APPLN. INFO.: | | | EP 2002-23906 | A 20021024 <-- |
| | | | US 2003-490285P | P 20030728 <-- |
| | | | WO 2003-EP11134 | W 20031008 <-- |

OTHER SOURCE(S): MARPAT 140:391200

AB ADB [D = methyleneurea moiety or derivative thereof; A = (substituted) L(ML')a; L = 5-7 membered cyclic structure, e.g. aryl, heteroaryl, arylene, heteroarylene; L' = (substituted) cyclic moiety having ≥5 members, e.g. aryl, heteroaryl, aralkyl, cycloalkyl, heterocyclyl; M = bond, bridging group having ≥1 atom; a = 1-4; B = (substituted) up to tricyclic aryl, heteroaryl], were prepared for treatment of hyperproliferative and nonproliferative disorders (no data). Thus, 4-(4-pyridinyloxy)benzylamine (preparation given) and 4-chloro-3-trifluoromethylphenyl isocyanate were stirred together for 2 h in CH₂Cl₂ to give 1-(4-chloro-3-trifluoromethylphenyl)-3-[4-(4-pyridinyloxy)benzyl]urea.

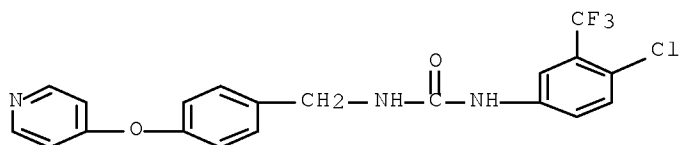
IT 685533-65-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of methylene urea derivs. as RAF kinase inhibitors)

RN 685533-65-7 HCAPLUS

CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[[4-(4-pyridinyloxy)phenyl]methyl]- (CA INDEX NAME)



IC ICM C07D213-00
 CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1
 IT 685533-65-7P 685533-66-8P 685533-67-9P 685533-68-0P
 685533-69-1P 685533-70-4P 685533-71-5P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 (preparation of methylene urea derivs. as RAF kinase inhibitors)
 IT 74-89-5, Methylamine, reactions 76-02-8, Trichloroacetyl chloride
 98-98-6, Pyridine-2-carboxylic acid 99-93-4, 4-Hydroxyacetophenone
 108-01-0, 2-Dimethylaminoethanol 109-00-2, 3-Hydroxypyridine 327-78-6,
 4-Chloro-3-trifluoromethylphenyl isocyanate 367-86-2,
 4-Fluoro-3-nitrobenzotrifluoride 619-24-9, 3-Nitrobenzonitrile
 626-55-1, 3-Bromopyridine 767-00-0, 4-Hydroxybenzonitrile 873-62-1,
 3-Hydroxybenzonitrile 6627-53-8, 5-Chloro-2-nitroanisole 55809-36-4,
 3-Amino-5-tert-butylisoxazole 56201-88-8 685534-00-3
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of methylene urea derivs. as RAF kinase inhibitors)

L110 ANSWER 30 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:203667 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 140:253554

TITLE: Preparation of pyridinyloxyphenylaminoacetamides as
 RAF kinase inhibitors

INVENTOR(S): Buchstaller, Hans-Peter; Wiesner, Matthias; Schadt,
 Oliver; Amendt, Christiane; Zenke, Frank; Sirrenberg,
 Christian; Grell, Matthias

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 182 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|--------------|
| WO 2004019941 | A1 | 20040311 | WO 2003-EP8474 | 20030731 <-- |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2496688 | A1 | 20040311 | CA 2003-2496688 | 20030731 <-- |
| AU 2003250197 | A1 | 20040319 | AU 2003-250197 | 20030731 <-- |

10/590724

EP 1531817 A1 20050525 EP 2003-790841 20030731 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 CN 1678314 A 20051005 CN 2003-820571 20030731 <--
 JP 2005539041 T 20051222 JP 2004-531844 20030731 <--
 US 20060167261 A1 20060727 US 2005-526043 20050228 <--
 PRIORITY APPLN. INFO.: EP 2002-19023 A 20020827 <--
 WO 2003-EP8474 W 20030731 <--

OTHER SOURCE(S): MARPAT 140:253554

AB ADB [D = (substituted) bivalent glycineamide moiety; A = L(ML1)a; L = 5-7
 membered cyclic structure, preferably aryl, heteroaryl, arylene,
 heteroarylene; L1 = (substituted) cyclic moiety having ≥5 members, preferably
 aryl, heteroaryl, aralkyl, cycloalkyl, heterocyclyl; M = bond, bridging group;
 a = 1-4; L, L1 contain 0-4 N, O, S atoms; B = (substituted) up to tricyclic
 aryl, heteroaryl containing 0-4 N, O, S atoms], were prepared for treatment of
 hyperproliferative and nonhyperproliferative disorders (no data). Thus, 3-(4-
 pyridinyloxy)aniline (preparation given), N-(5-tert-butyl-3-isoxazolyl)-2-
 chloroacetamide (preparation given), and diisopropylethylamine were heated in
 DMF at 100° for 4 h to give 48% N-(5-tert-butyl-3-isoxazolyl)-2-[3-(4-
 pyridinyloxy)phenylamino]acetamide.

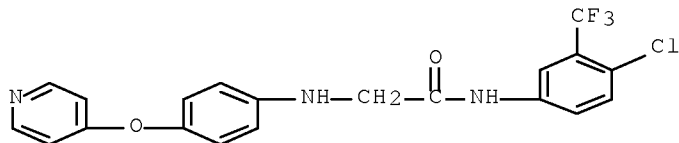
IT 668980-73-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of pyridinyloxyphenylaminoacetamides as RAF kinase inhibitors)

RN 668980-73-2 HCAPLUS

CN Acetamide, N-[4-chloro-3-(trifluoromethyl)phenyl]-2-[[4-(4-
 pyridinyloxy)phenyl]amino]- (CA INDEX NAME)



IC ICM A61K031-4409

ICS A61K031-4427; C07D213-68; C07D413-12; A61P035-00

CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1, 27

IT 668980-73-2P 668980-74-3P 668980-75-4P 668980-76-5P
 668980-77-6P 668980-78-7P 668980-79-8P 668980-80-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of pyridinyloxyphenylaminoacetamides as RAF kinase inhibitors)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 31 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:533967 HCAPLUS Full-text

DOCUMENT NUMBER: 141:65147

TITLE: Method for treating diseases associated with abnormal
 tyrosine kinase activity by administering a DNA
 methylation inhibitor and a tyrosine kinase inhibitor

INVENTOR(S): Lyons, John; Rubinfeld, Joseph

PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of U.S. Ser. No. 71,849.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-----------------|
| US 20040127453 | A1 | 20040701 | US 2002-206854 | 20020726 <-- |
| US 6998391 | B2 | 20060214 | | |
| US 20030147813 | A1 | 20030807 | US 2002-71849 | 20020207 <-- |
| CA 2474174 | A1 | 20030814 | CA 2003-2474174 | 20030206 <-- |
| WO 2003065995 | A2 | 20030814 | WO 2003-US3537 | 20030206 <-- |
| WO 2003065995 | A3 | 20051013 | | |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2003215065 | A1 | 20030902 | AU 2003-215065 | 20030206 <-- |
| EP 1572075 | A2 | 20050914 | EP 2003-710881 | 20030206 <-- |
| EP 1572075 | A3 | 20051207 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| US 20060140947 | A1 | 20060629 | US 2005-181368 | 20050713 <-- |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 2002-71849 | A2 20020207 <-- |
| | | | US 2002-206854 | A 20020726 <-- |
| | | | WO 2003-US3537 | W 20030206 <-- |

AB Methods are provided for treating diseases associated with abnormal activity of kinases. The method comprises: administering a DNA methylation inhibitor to the patient in therapeutically effective amount; and administering a kinase inhibitor to the patient in therapeutically effective amount, such that the in vivo activity of the kinase is reduced relative to that prior to the treatment. The method can be used to treat cancer associated with abnormal activity of kinases such as phosphatidylinositol 3'-kinase (PI3K), protein kinases including serine/threonine kinases such as Raf kinases, protein kinase kinases such as MEK, and tyrosine kinases such as those in the epidermal growth factor receptor family (EGFR), platelet-derived growth factor receptor family (PDGFR), vascular endothelial growth factor receptor (VEGFR) family, nerve growth factor receptor family (NGFR), fibroblast growth factor receptor family (FGFR) insulin receptor family, ephrin receptor family, Met family, Ror family, c-kit family, Src family, Fes family, JAK family, Fak family, Btk family, Syk/ZAP-70 family, and Abl family.

IT 284461-73-0, BAY 43-9006

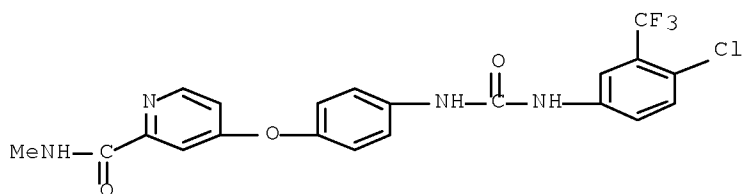
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);

THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Raf kinase inhibitor; treating diseases associated with abnormal tyrosine kinase activity by administering DNA methylation inhibitors and tyrosine kinase inhibitors)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K031-7072
 INCL 514050000
 CC 1-12 (Pharmacology)
 Section cross-reference(s): 7
 IT 284461-73-0, BAY 43-9006
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (Raf kinase inhibitor; treating diseases associated with abnormal tyrosine
 kinase activity by administering DNA methylation inhibitors and
 tyrosine kinase inhibitors)
 REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 32 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:513393 HCAPLUS Full-text
 DOCUMENT NUMBER: 141:71544
 TITLE: Preparation of substituted benzazoles as Raf kinase
 inhibitors
 INVENTOR(S): Amiri, Payman; Fantl, Wendy; Levine, Barry Haskell;
 Poon, Daniel J.; Ramurthy, Savithri; Renhowe, Paul A.;
 Subramanian, Sharadha; Sung, Leonard
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 476 pp., Cont.-in-part of U.S.
 Pat. Appl. 2004 87,626.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------|------|----------|-----------------|--------------|
| US 20040122237 | A1 | 20040624 | US 2003-675927 | 20030929 <-- |
| US 20040087626 | A1 | 20040506 | US 2003-405945 | 20030331 <-- |
| US 7071216 | B2 | 20060704 | | |
| AU 2004277405 | A1 | 20050414 | AU 2004-277405 | 20040929 <-- |
| CA 2539748 | A1 | 20050414 | CA 2004-2539748 | 20040929 <-- |
| WO 2005032548 | A1 | 20050414 | WO 2004-US32161 | 20040929 <-- |

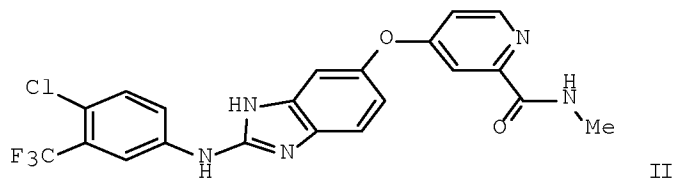
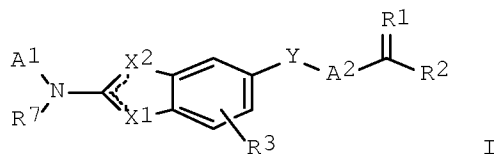
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,

10/590724

EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

| | | | | |
|--|----|----------|------------------|-----------------|
| EP 1675584 | A1 | 20060705 | EP 2004-789345 | 20040929 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| BR 2004014908 | A | 20061107 | BR 2004-14908 | 20040929 <-- |
| CN 1913884 | A | 20070214 | CN 2004-80032677 | 20040929 <-- |
| JP 2007507428 | T | 20070329 | JP 2006-528331 | 20040929 <-- |
| US 20070299039 | A1 | 20071227 | US 2005-282939 | 20051118 <-- |
| MX 2006PA03435 | A | 20060620 | MX 2006-PA3435 | 20060327 <-- |
| JP 2006193533 | A | 20060727 | JP 2006-96143 | 20060330 <-- |
| IN 2006KN00838 | A | 20070413 | IN 2006-KN838 | 20060405 <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-369066P | P 20020329 <-- |
| | | | US 2003-405945 | A2 20030331 <-- |
| | | | JP 2003-579810 | A3 20030331 <-- |
| | | | US 2003-675927 | A 20030929 <-- |
| | | | WO 2004-US32161 | W 20040929 |

OTHER SOURCE(S): MARPAT 141:71544
GI



AB The title compds. I [wherein X1, X2 = N, NR4, O, S (with provisos); Y = O, S; A1 = (un)substituted alkyl, (hetero)cycloalkyl(alkyl), (hetero)aryl(alkyl), etc.; A2 = (un)substituted heteroaryl; R1 = O, H; R2 = NR5R6, OH; or CR1R2 = (un)substituted heterocycloalkyl, heteroaryl; R3 = H, halo, alkyl, alkoxy; R4 = H, OH, (di)alkylamino, alkyl; R5, R6 = H, (un)substituted (cyclo)alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, heterocyclyl, (hetero)aryl, etc.; or R5 and R6 are taken together to form (un)substituted heterocyclyl or heteroaryl; R7 = alkyl; and pharmaceutically acceptable salts, esters, or prodrugs] were prepared as Raf kinase inhibitors. Examples include synthetic methods and phys. data for 1400 compds., as well as descriptions of two Raf kinase bioassays. For instance, 4-amino-3-nitrophenol and (4-chloropyridin-2-yl)-N-methylcarboxamide were coupled using potassium bis(trimethylsilyl)amide and K2CO3 in DMF to give 4-[(4-amino-3-nitrophenyl)oxy]-N-methylpyridine-2-carboxamide. Pd-catalyzed hydrogenation, followed by cyclization with 4-chloro-3-(trifluoromethyl)benzeneisothiocyanate in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide•HCl in THF provided the benzimidazole II. One thousand ninety-four compds. inhibited Raf kinase activity with IC50 < 5 μM in a Raf/Mek filtration assay or a biotinylated Raf screen. Thus, I and

10/590724

their pharmaceutical compns., which may comprise at least one addnl. agent, are useful for the treatment of Raf kinase mediated disorders, such as cancer (no data).

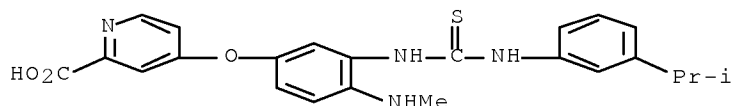
IT 611225-97-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of substituted benzazoles as Raf kinase inhibitors for treatment of cancer)

RN 611225-97-9 HCAPLUS

CN 2-Pyridinecarboxylic acid, 4-[4-(methyamino)-3-[[[3-(1-methylethyl)phenyl]amino]thioxomethyl]amino]phenoxy]- (CA INDEX NAME)



IC ICM C07D277-82

ICS C07D263-60

INCL 548161000; 548217000

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

IT 656-64-4P 823-54-1P 3530-00-5P, 3-Phenoxyphenylisothiocyanate
 6358-77-6P 7748-59-6P 7748-60-9P 20734-76-3P 23491-48-7P
 49559-34-4P 49559-83-3P 54998-08-2P 79110-05-7P 106146-35-4P
 114780-06-2P 115619-00-6P 115619-01-7P 120381-42-2P 127142-66-9P,
 (4-Chloro-3-nitrophenyl)isothiocyanate 129488-00-2P 191602-42-3P
 191602-43-4P, (3-Bromo-4-isopropoxyphenyl)amine 210158-20-6P
 211635-75-5P 214337-39-0P 219552-64-4P 220000-86-2P 239122-51-1P
 262368-47-8P 284462-57-3P 284462-58-4P 401815-98-3P 402948-23-6P
 402948-25-8P 402948-26-9P 414880-35-6P 483324-01-2P 485841-45-0P
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 710351-29-4P 710351-30-7P 710351-32-9P 710351-65-8P 710351-66-9P
 710351-70-5P, 1-(2-Methyl-5-nitrophenyl)pyrrolidine 710351-71-6P,
 [4-Methyl-3-(pyrrolidin-1-yl)phenyl]amine 710351-72-7P,
 [4-Methyl-3-(pyrrolidin-1-yl)phenyl]isothiocyanate 710351-74-9P,
 4-[[2-[(4-Chloro-3-nitrophenyl)amino]-1-methylbenzimidazol-5-yl]oxy]-N-
 methylpyridine-2-carboxamide 710351-75-0P, 4-[[2-[(3-Amino-4-
 chlorophenyl)amino]-1-methylbenzimidazol-5-yl]oxy]-N-methylpyridine-2-

carboxamide 710351-78-3P, 4-[4-(Methylamino)-3-nitrophenoxy]pyridine-2-
 carboxamide 710351-79-4P, 4-[3-Amino-4-(methylamino)phenoxy]pyridine-2-
 carboxamide 710351-81-8P, 1-[2-(3-Nitrophenyl)ethyl]pyrrolidine
 710351-82-9P, [3-[2-(Pyrrolidin-1-yl)ethyl]phenyl]amine 710351-83-0P,
 [3-[2-(Pyrrolidin-1-yl)ethyl]phenyl]isothiocyanate 710351-84-1P,
 [3-Bromo-4-(2,2,2-trifluoroethoxy)phenyl]amine 710351-85-2P,
 2-Bromo-4-nitro-1-(2,2,2-trifluoroethoxy)benzene 710351-86-3P,
 3-Isopropyl-4-fluoroaniline 710351-87-4P, 4-Methyl-3-(3-
 furyl)nitrobenzene 710351-88-5P, 4-Methyl-3-(3-furyl)aniline
 710351-89-6P, 4-Methyl-3-(tetrahydrofuran-3-yl)aniline
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (intermediate; preparation of substituted benzazoles as Raf kinase
 inhibitors for treatment of cancer)

L110 ANSWER 33 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:433797 HCAPLUS Full-text

DOCUMENT NUMBER: 140:423477

TITLE: Preparation of diaryl ureas as inhibitors of p38
 kinase

INVENTOR(S): Miller, Scott; Osterhout, Martin; Dumas, Jacques;
 Khire, Uday; Lowinger, Timothy B.; Scott, William J.;
 Smith, Roger A.; Wood, Jill E.; Gunn, David E.;
 Hatoum-Mokdad, Holia; Rodriguez, Marell; Sibley,
 Robert; Wang, Ming; Turner, Tiffany; Brennan,
 Catherine

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 60 pp., Cont. of U.S. Ser. No.
 458,015, abandoned.
 CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-----------------|
| US 20040102636 | A1 | 20040527 | US 2002-60396 | 20020201 <-- |
| PRIORITY APPLN. INFO.: | | | US 1997-126439P | P 19971222 <-- |
| | | | US 1998-285522 | B1 19981222 <-- |
| | | | US 1999-458015 | B1 19991210 <-- |

OTHER SOURCE(S): MARPAT 140:423477

AB A method of treating a p-38 mediated disease other than cancer comprises
 administration of BNHCONHA [A = (substituted) Ph, pyridyl, 2-thienyl; B =
 (substituted) aryl, heteroaryl containing ≥ 1 6-membered aromatic structure
 containing 0-4 N, O, or S atoms]. Thus, 5-tert-butyl-2-(3-
 tetrahydrofuranyloxy)aniline (preparation given) and p-tolyl isocyanate were
 stirred 8 h in PhMe to give 75% N-(5-tert-butyl-2-(3-
 tetrahydrofuranyloxy)phenyl)-N'-(4-methylphenyl)urea. Title compds. inhibited
 p38 kinase with IC₅₀ = 1-10 μ M.

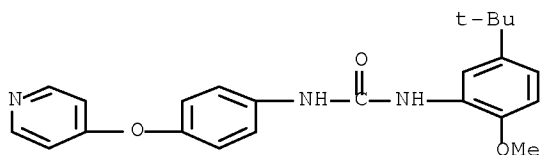
IT 228399-41-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of diaryl ureas as inhibitors of p38 kinase)

RN 228399-41-5 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-(4-
 pyridinyloxy)phenyl]- (CA INDEX NAME)



IC ICM A61K031-44
 ICS A61K031-381; A61K031-325; A61K031-277; A61K031-17; A61K031-216;
 A61K031-195

INCL 546306000; 549069000; 558418000; 560024000; 564050000; 564049000;
 514349000; 514447000; 514485000; 514522000

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
 Section cross-reference(s): 1, 27, 28, 63

IT 370-50-3P 117745-34-3P 228399-32-4P 228399-33-5P 228399-34-6P
 228399-35-7P 228399-38-0P ~~228399-41-5P~~ ~~228399-44-8P~~
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of diaryl ureas as inhibitors of p38 kinase)

L110 ANSWER 34 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:182368 HCAPLUS Full-text

DOCUMENT NUMBER: 140:229401

TITLE: Three hybrid assay system for isolating ligand-binding

10/590724

INVENTOR(S): polypeptides and for isolating small mol. ligands
Come, Jon H.; Becker, Frank; Kley, Nikolai A.;
Reichel, Christoph
PATENT ASSIGNEE(S): Gpc Biotech Inc., USA; Gpc Biotech AG
SOURCE: U.S. Pat. Appl. Publ., 238 pp., Cont.-in-part of U.S.
Ser. No. 91,177.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

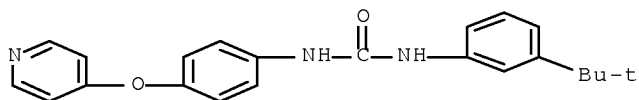
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|-----------------|
| US 20040043388 | A1 | 20040304 | US 2002-234985 | 20020903 <-- |
| US 7135550 | B2 | 20061114 | | |
| US 20030165873 | A1 | 20030904 | US 2002-91177 | 20020304 <-- |
| EP 1832589 | A1 | 20070912 | EP 2007-8359 | 20021015 <-- |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, SK, TR, AL, LT, LV, MK | | | | |
| US 20040266854 | A1 | 20041230 | US 2004-820453 | 20040407 <-- |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 2001-272932P | P 20010302 <-- |
| | | | US 2001-278233P | P 20010323 <-- |
| | | | US 2001-329437P | P 20011015 <-- |
| | | | US 2002-91177 | A2 20020304 <-- |
| | | | US 2001-336962P | P 20011203 <-- |
| | | | WO 2002-US6677 | A2 20020304 <-- |
| | | | US 2002-234985 | A2 20020903 <-- |
| | | | EP 2002-797047 | A3 20021015 <-- |
| | | | WO 2002-US33052 | A2 20021015 <-- |
| | | | US 2003-460921P | P 20030407 <-- |
| | | | US 2003-531872P | P 20031223 <-- |

AB The invention provides compns. and methods for isolating ligand-binding polypeptides for a user-specified ligand, and for isolating small mol. ligands for a user-specified target polypeptide using an improved class of hybrid ligand compds. Preparation of compds., e.g a methotrexate moiety linked by a polyethylene glycol moiety to dexamethasone, is described.

IT 228399-50-6D, conjugates
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(three hybrid assay system for isolating ligand-binding polypeptides and for isolating small mol. ligands)

RN 228399-50-6 HCAPLUS

CN Urea, N-[3-(1,1-dimethylethyl)phenyl]-N'-[4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME)



IC ICM C12Q001-68
ICS G01N033-53; C07H021-04
INCL 435006000; X43-5 .71; X53-6 2.31; X53-035.0; X55-265.3; X55-250.0;
X53-612.3; X54-6 .1; X54-020.0; X53-031.7
CC 1-1 (Pharmacology)

Section cross-reference(s): 9, 28

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 413599-62-9D, conjugates 431916-96-0D, conjugates

RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(three hybrid assay system for isolating ligand-binding polypeptides
 and for isolating small mol. ligands)

L110 ANSWER 35 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:950982 HCAPLUS Full-text

DOCUMENT NUMBER: 140:16736

TITLE: Preparation of diarylurea derivatives useful for the
 treatment of protein kinase dependent diseases

INVENTOR(S): Floersheimer, Andreas; Furet, Pascal; Manley, Paul
 William; Bold, Guido; Boss, Eugen; Guagnano, Vito;
 Vaupel, Andrea

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.

SOURCE: PCT Int. Appl., 170 pp.

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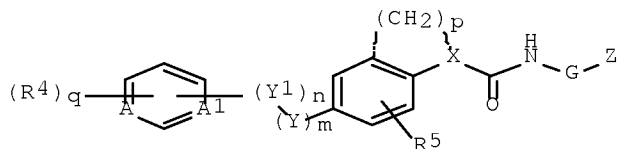
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|--------------|
| ----- | ---- | ----- | ----- | ----- |
| WO 2003099771 | A2 | 20031204 | WO 2003-EP5634 | 20030528 <-- |

WO 2003099771 A3 20040401

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW
 RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

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|---|----|----------|-----------------|----------------|
| CA 2484288 | A1 | 20031204 | CA 2003-2484288 | 20030528 <-- |
| AU 2003242591 | A1 | 20031212 | AU 2003-242591 | 20030528 <-- |
| AU 2003242591 | B2 | 20070726 | | |
| BR 2003011313 | A | 20050215 | BR 2003-11313 | 20030528 <-- |
| EP 1511730 | A2 | 20050309 | EP 2003-755147 | 20030528 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN 1656073 | A | 20050817 | CN 2003-812280 | 20030528 <-- |
| JP 2005527622 | T | 20050915 | JP 2004-507429 | 20030528 <-- |
| NZ 536781 | A | 20071221 | NZ 2003-536781 | 20030528 <-- |
| ZA 2004008314 | A | 20060726 | ZA 2004-8314 | 20041014 <-- |
| IN 2004CN02670 | A | 20070720 | IN 2004-CN2670 | 20041125 <-- |
| MX 2004PA11789 | A | 20050331 | MX 2004-PA11789 | 20041126 <-- |
| NO 2004005521 | A | 20041217 | NO 2004-5521 | 20041217 <-- |
| US 20060128734 | A1 | 20060615 | US 2005-515113 | 20051208 <-- |
| PRIORITY APPLN. INFO.: | | | GB 2002-12413 | A 20020529 <-- |
| | | | GB 2003-5684 | A 20030312 <-- |
| | | | GB 2003-9219 | A 20030423 <-- |
| | | | WO 2003-EP5634 | W 20030528 <-- |

OTHER SOURCE(S): MARPAT 140:16736
 GI



I

AB The invention relates to the use of diaryl urea derivs. [I; G is not present and Z = a radical of the formula Q; A = CH, N, N→O; A1 = N, N→O, with the proviso that not more than one of A and A1 can be N→O; n = 1, 2; m = 0-2; p = 0, 2, 3; q = 0-5; X = (un)substituted NH if p = 0; or if p is 2 or 3, X = nitrogen which together with (CH2)p and the bonds represented in dotted (interrupted) lines (including the atoms to which they are bound) forms a ring, or X = CHK (wherein K = H or lower alkyl) and p = 0, with the proviso that the bonds represented in dotted lines, if p = 0, are absent; Y1 = O, S, CH2; Y2 = O, S, NH; with the proviso that (Y1)n-(Y2)m does not include O-O, S-S, NH-O, NH-S or S-O groups; R1, R2, R3, R5 = independently H or an inorg. or organic moiety or any two of them together form a lower alkylenedioxy bridge bound via the oxygen atoms, and the remaining one of these moieties is hydrogen or an inorg. or organic moiety; R4 (if present, i.e., if q is not zero) is an inorg. or organic moiety] or tautomers thereof or pharmaceutically acceptable salts thereof in the treatment of protein kinase dependent diseases or for the manufacture of pharmaceutical compns. for use in the treatment of said diseases, especially a proliferative disease depending on any one or more

of the following (tyrosine) protein kinases such as ras, Abl, VEGF-receptor tyrosine kinase, Flt3, and/or Bcr-Abl activity. Also disclosed are the use of the compds. I for the manufacture of pharmaceutical compns. for use in the treatment of said diseases, methods of use of the compds. I in the treatment of said diseases, pharmaceutical preps. comprising the compds. I for the treatment of said diseases, processes for the manufacture of the compds. I, the use or methods of use of the compds. I as mentioned above, and/or the compds. I for use in the treatment of the animal or human body. For example, N-(4-(pyridin-4-yloxy)phenyl)-N'-(4-2,2,2-trifluoroethoxy-3-trifluoromethylphenyl)urea and N-[4-[6-(4-hydroxyphenylamino)pyrimidin-4-yl]phenyl]-N'-(4-2,2,2-trifluoroethoxy-3-trifluoromethylphenyl)urea at 10 μ M inhibited gene c-Abl protein kinase by 98%, Kdr receptor tyrosine kinase by 100 and 96%, resp., and Flt3 receptor tyrosine kinase by 100%.

IT 630125-50-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

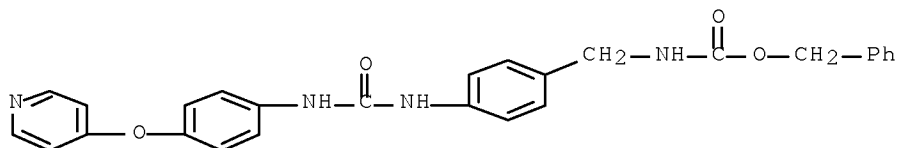
(intermediate; preparation of diarylurea derivs. useful for the treatment

of

protein kinase dependent diseases and proliferative diseases)

RN 630125-50-7 HCAPLUS

CN Carbamic acid, [[4-[[[4-(4-pyridinyloxy)phenyl]amino]carbonyl]amino]phenyl]methyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



IC ICM C07C275-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 7, 27, 63

IT 393-15-7P, 4-Methoxy-3-trifluoromethylphenylamine 2802-62-2P, 4,6-Difluoropyrimidine 15862-01-8P, 2-Methoxy-4-nitrobiphenyl 20566-90-9P, 3-Nitro-N,N-dimethyl-5-trifluoromethylbenzamide 22227-42-5P, (Piperidin-1-yl)(3-nitro-5-trifluoromethylphenyl)methanone 56970-24-2P, 2-Methoxybiphenyl-4-ylamine 58609-19-1P 70339-06-9P, 4-Piperidin-1-yl-3-trifluoromethylphenylamine 102877-78-1P, 4-(Pyridin-4-yloxy)phenylamine 105130-28-7P, 4-(6-Chloropyrimidin-4-yloxy)aniline 105296-03-5P 105298-89-3P 105350-42-3P 118450-89-8P, 1-(2-Methoxy-4-nitrophenyl)piperidine 124041-03-8P, 4-Chloro-6-(4-nitrophenoxy)pyrimidine 168050-39-3P, (4-Aminobenzyl)carbamic acid benzyl ester 186090-34-6P 252918-98-2P 260783-12-8P, (4-Chloropyridin-2-yl)pyrrolidin-1-ylmethanone 330796-48-0P, 4-(4-Methylpiperazin-1-yl)-3-trifluoromethylphenylamine 417724-25-5P, 6-(4-Aminophenoxy)pyrimidin-4-ylamine 630125-30-3P, Methyl[4-(pyridin-4-yloxy)phenyl]amine 630125-32-5P, N-(4-Ethylphenyl)-2-(4-hydroxyphenyl)acetamide 630125-33-6P 630125-34-7P, 5-(Pyridin-4-yloxy)-2,3-dihydroindole 630125-35-8P, 6-(Pyridin-4-yloxy)-1,2,3,4-tetrahydroquinoline 630125-36-9P, 6-(Pyridin-4-yloxy)quinoline 630125-37-0P 630125-38-1P, [6-(4-Aminophenoxy)pyrimidin-4-yl][4-(tert-butyl dimethylsilyloxy)phenyl]amine 630125-39-2P, [4-(tert-butyl dimethylsilyloxy)phenyl][6-(4-nitrophenoxy)pyrimidin-4-yl]amine 630125-40-5P, 4-[6-(4-Nitrophenoxy)pyrimidin-4-ylamino]phenol 630125-41-6P, 3-Chloro-4-(pyridin-4-yloxy)phenylamine 630125-43-8P,

[6-(4-Aminophenoxy)pyrimidin-4-yl](4-methoxyphenyl)amine 630125-44-9P,
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 630125-46-1P 630125-47-2P 630125-48-3P ~~630125-50-7P~~
 630125-51-8P, [4-(Benzyloxycarbonylaminomethyl)phenyl]carbamic acid
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 6-(4-Aminobenzyl)pyrimidin-4-ylamine 630126-14-6P, [4-(6-Aminopyrimidin-
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 [4-(6-Azidopyrimidin-4-ylmethyl)phenyl]carbamic acid tert-butyl ester
 630126-16-8P, 5-(6-Chloropyrimidin-4-yloxy)-1H-indole 630126-17-9P,
 5-(6-Chloropyrimidin-4-yloxy)-2,3-dihydro-1H-indole

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of diarylurea derivs. useful for the treatment

of

protein kinase dependent diseases and proliferative diseases)

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 630123-49-8P 630123-51-2P 630123-53-4P 630123-55-6P 630123-56-7P
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 3-ylmethyl)phenyl]-N'-(4-methylphenyl)urea 630123-91-0P 630123-92-1P
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~~630125-27-8P 630125-28-9P 630125-29-0P~~

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of diarylurea derivs. useful for the treatment of protein
 kinase dependent diseases and proliferative diseases)

L110 ANSWER 36 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:796477 HCAPLUS Full-text

DOCUMENT NUMBER: 139:307759

TITLE: Preparation of substituted benzazoles as Raf kinase inhibitors

INVENTOR(S): Renhowe, Paul A.; Ramurthy, Savithri; Amiri, Payman; Levine, Barry Haskell; Poon, Daniel J.; Subramanian, Sharadha; Sung, Leonard; Fantl, Wendy

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: PCT Int. Appl., 259 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

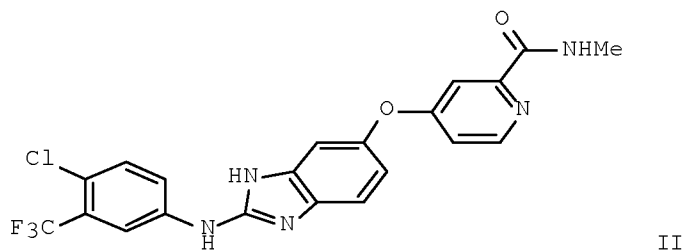
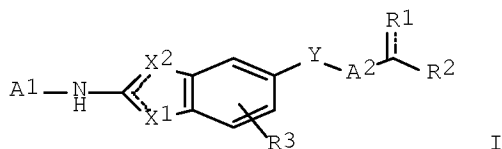
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|--|--------------|
| ----- | ---- | ----- | ----- | ----- |
| WO 2003082272 | A1 | 20031009 | WO 2003-US10117 | 20030331 <-- |
| W: | | | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | |
| RW: | | | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | |
| CA 2480638 | A1 | 20031009 | CA 2003-2480638 | 20030331 <-- |
| AU 2003226211 | A1 | 20031013 | AU 2003-226211 | 20030331 <-- |
| AU 2003226211 | B2 | 20080529 | | |

10/590724

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| EP 1499311 | A1 | 20050126 | EP 2003-745683 | 20030331 <-- |
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| BR 2003008854 | A | 20050222 | BR 2003-8854 | 20030331 <-- |
| CN 1655779 | A | 20050817 | CN 2003-812193 | 20030331 <-- |
| JP 2005529089 | T | 20050929 | JP 2003-579810 | 20030331 <-- |
| NZ 535985 | A | 20070427 | NZ 2003-535985 | 20030331 <-- |
| IN 2004KN01433 | A | 20051230 | IN 2004-KN1433 | 20040927 <-- |
| MX 2004PA09541 | A | 20050125 | MX 2004-PA9541 | 20040929 <-- |
| NO 2004004617 | A | 20041228 | NO 2004-4617 | 20041026 <-- |
| ZA 2004008386 | A | 20060531 | ZA 2004-8386 | 20060308 <-- |
| JP 2006193533 | A | 20060727 | JP 2006-96143 | 20060330 <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-369066P | P 20020329 <-- |
| | | | JP 2003-579810 | A3 20030331 <-- |
| | | | WO 2003-US10117 | W 20030331 <-- |

OTHER SOURCE(S): MARPAT 139:307759

GI



AB The title compds. [I; X1, X2 = N, NR4, O, S (with the provisos); Y = O, S; A1 = (un)substituted alkyl, cycloalkyl, aryl, etc.; A2 = (un)substituted heteroaryl; R1 = O, H, and R2 = NR5R6, OH; or CR1R2 = (un)substituted heterocycloalkyl, heteroaryl; R3 = H, halo, alkyl, alkoxy; R4 = H, OH, (di)alkylamino, alkyl; R5, R6 = H, (un)substituted alkyl, alkoxyalkyl, etc.; or R5 and R6 are taken together to form (un)substituted heterocyclyl or heteroaryl], useful for inhibition of Raf kinase activity in a human or animal subject, were prepared E.g., a 3-step synthesis of the benzimidazole II (starting from 4-amino-3-nitrophenol and (4-chloropyridin-2-yl)-N-methylcarboxamide), was given. The compds. of examples 1-1094 showed a Raf kinase inhibitory activity at an IC50 of less than 5 μ M. A composition comprising the compound I is claimed. The new compds. compns. may be used either alone or in combination with at least one addnl. agent for the treatment of a Raf kinase mediated disorder, such as cancer.

IT 611225-97-9P

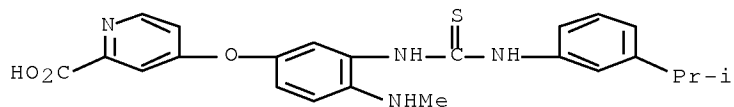
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

 (preparation of substituted benzazoles as Raf kinase inhibitors)

RN 611225-97-9 HCAPLUS

10/590724

CN 2-Pyridinecarboxylic acid, 4-[4-(methylamino)-3-[[[3-(1-methylethyl)phenyl]amino]thioxomethyl]amino]phenoxy]- (CA INDEX NAME)



IC ICM A61K031-41
ICS C07D401-12; C07D405-14; C07D409-14; C07D401-14; C07D417-12;
C07D417-14; C07D413-14; C07D407-14; C07D413-12; C07D471-08;
A61P035-00

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 53

IT 823-54-1P 3530-00-5P, 3-Phenoxyphenylisothiocyanate 7748-59-6P
7748-60-9P 20734-76-3P 23491-48-7P 49559-34-4P 49559-83-3P
54998-08-2P 106146-35-4P 114780-06-2P 115619-00-6P 115619-01-7P
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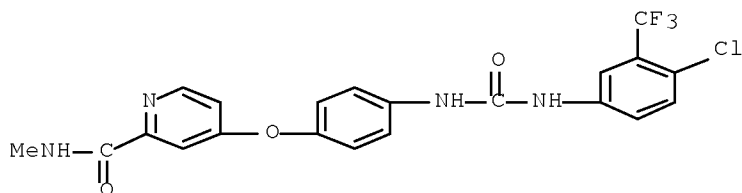
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of substituted benzazoles as Raf kinase inhibitors)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 37 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737931 HCAPLUS Full-text
DOCUMENT NUMBER: 139:255332
TITLE: Method for selecting antitumor drug
sensitivity-determining factors and method for
predicting antitumor drug sensitivity using the
selected factors
INVENTOR(S): Aoki, Yuko; Hasegawa, Kiyoshi; Ishii, Nobuya; Mori,
Kazushige
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|-----------------|----------------|
| WO 2003076660 | A1 | 20030918 | WO 2002-JP2354 | 20020313 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2478640 | A1 | 20030918 | CA 2002-2478640 | 20020313 <-- |
| AU 2002238874 | A1 | 20030922 | AU 2002-238874 | 20020313 <-- |
| EP 1483401 | A1 | 20041208 | EP 2002-705127 | 20020313 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| CN 1625602 | A | 20050608 | CN 2002-828958 | 20020313 <-- |
| JP 2005519610 | T | 20050707 | JP 2003-574857 | 20020313 <-- |
| US 20050118600 | A1 | 20050602 | US 2005-507389 | 20050120 <-- |
| PRIORITY APPLN. INFO.: | | | WO 2002-JP2354 | W 20020313 <-- |
| AB | Based on drug sensitivity data and extensive gene expression data, a model was constructed by multivariate anal. with the partial least squares method type 1. Further, the model was optimized using modeling power and genetic algorithm. Thereby, the degree of contribution of the resp. genes to drug sensitivity was determined to select genes with a high degree of contribution. In addition, the levels of gene expression in specimens were analyzed, and then the drug sensitivity was predicted based on the model. The predicted values agreed well with those drug sensitivity values determined exptl. The drug sensitivity-predicting method provided by the present invention enables assessment of the effectiveness of a drug prior to administration using small quantities of specimens associated with diseases such as cancer. Since this enables the selection of the most suitable drug for each patient, the present invention is very useful in improving a patient's quality of life (QOL). | | | |
| IT | 284461-73-0, BAY 439006 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (method for selecting antitumor drug sensitivity-determining factors and predicting antitumor drug sensitivity using the selected factors) | | | |
| RN | 284461-73-0 HCAPLUS | | | |
| CN | 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c arboxyl]amino]phenoxy]-N-methyl- (CA INDEX NAME) | | | |



IC ICM C12Q001-68
ICS G06K009-62; G06F017-17
CC 1-6 (Pharmacology)
Section cross-reference(s): 2
IT 51-21-8, 5-FU 66-22-8, 2,4(1H,3H)-Pyrimidinedione, biological studies
147-94-4, Ara-C 2207-75-2, Potassium oxonate 2353-33-5, Decitabine
3094-09-5, Furtulon 4291-63-8, Cladribine 7689-03-4, Camptothecin
10540-29-1, Tamoxifen 15663-27-1, Cisplatin 17902-23-7, Tegafur
20830-81-3, Daunomycin 25316-40-9, Adriamycin 33069-62-4, Taxol
41575-94-4, Carboplatin 53714-56-0, Leuprorelin 56420-45-2, Epirubicin
58957-92-9, Idarubicin 61422-45-5, Carmofur 75607-67-9 82640-04-8,
LY156758 90357-06-5, ZD 176334 91421-42-0, 9-Nitrocamptothecin
91421-43-1, 9-Aminocamptothecin 100286-90-6, CPT-11 103766-25-2,
5-Chloro-2,4-dihydroxypyridine 105149-00-6, TZP4238 107868-30-4,
FCE24304 110417-88-4, Dolastatin 10 112809-51-5, CGS 20267
114977-28-5, Taxotere 115767-74-3, TAT59 119804-96-5, DMDC
120511-73-1, ZD 1033 120685-11-2, CGP41251 123884-00-4, Dolastatin 15
123948-87-8, Topotecan 126723-15-7, Dolastatin 14 145918-75-8,
Troxacitabine 149606-27-9, TZT 1027 154361-50-9, Xeloda 159776-69-9,
Cemadotin 160237-25-2, BMS 184476 169869-90-3, DX-8951f 171179-06-9,
PD 158780 172481-83-3, BMS 188797 172903-00-3, BBR 3464 182133-25-1,
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1839 186348-23-2, IDN 5109 189453-10-9, Epothilone D 192185-68-5,
R115777 193275-84-2, SCH66336 195987-41-8, BMS 214662 204005-46-9,
SU5416 212142-18-2, PTK787 212631-79-3, CI1040 219989-84-1, BMS
247550 220127-57-1, STI-571 220997-97-7, BN-80915 252916-29-3,
SU6668 253863-00-2, L778123 284461-73-0, BAY 439006
437755-78-7, GW 2016 443913-73-3, ZD6474 601517-74-2, GW 2286
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(method for selecting antitumor drug sensitivity-determining factors and
predicting antitumor drug sensitivity using the selected factors)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 38 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:656745 HCAPLUS Full-text

DOCUMENT NUMBER: 139:197377

TITLE: Preparation of aryl ureas for therapeutic use as
kinase inhibitors

INVENTOR(S): Dumas, Jacques; Scott, William J.; Chien, Du-Schieng;
Lee, Wendy; Bjorge, Susan; Musza, Laszlo L.; Nassar,
Ala; Riedl, Bernd

PATENT ASSIGNEE(S): Bayer Corporation, USA; Bayer Pharmaceuticals
Corporation

SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

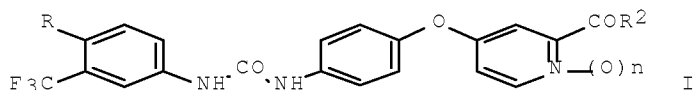
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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|---------------|---|----------|-----------------|--------------|
| WO 2003068746 | A1 | 20030821 | WO 2003-US4109 | 20030211 <-- |
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10/590724

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
 UG, US, UZ, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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 AU 2003209118 A1 20030904 AU 2003-209118 20030211 <--
 US 20030216446 A1 20031120 US 2003-361859 20030211 <--
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 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 CN 1630638 A 20050622 CN 2003-803705 20030211 <--
 JP 2005523278 T 20050804 JP 2003-567877 20030211 <--
 EP 1580188 A1 20050928 EP 2005-7027 20030211 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, FI, CY, TR, BG, CZ, EE, HU, SK
 MX 2004PA07830 A 20050701 MX 2004-PA7830 20040811 <--
 HK 1079774 A1 20071221 HK 2005-111827 20051222 <--
 PRIORITY APPLN. INFO.: US 2002-354937P P 20020211 <--
 EP 2003-707848 A3 20030211 <--
 WO 2003-US4109 W 20030211 <--
 OTHER SOURCE(S): MARPAT 139:197377
 GI

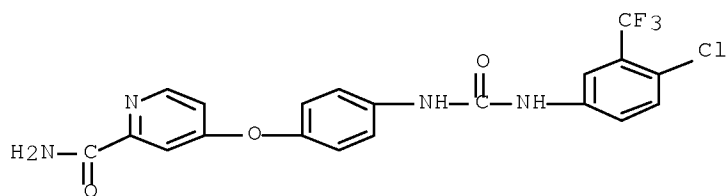


AB Aryl ureas, such as I [R = Cl, Br; R2 = OH, NH2, NHMe, NHCH2OH, alkoxy; n = 0, 1], were prepared for use in pharmaceutical compns. for the treatment of raf kinase and p38 kinase mediated diseases. These ureas are useful for the treatment of inflammation, osteoporosis, angiogenesis disorders and hyper-proliferative disorders, such as cancer. Thus, urea I (R = Cl, R2 = NHMe, n = 1) was prepared with 57% yield by N-oxidation of I (R = Cl, R2 = NHMe, n = 0) using 3-chloroperbenzoic acid in CH2Cl2 and THF. The prepared ureas were assayed for inhibition of p38 kinase and raf kinase, as well as for cancer cell growth inhibition in human cancer cell lines, such as HCT116 and DLD-1.

IT 284461-74-1P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-carbamoyl(4-pyridyloxy)phenyl]urea
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation of aryl ureas for therapeutic use as kinase inhibitors)

RN 284461-74-1 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c carbonyl]amino]phenoxy]- (CA INDEX NAME)



IC ICM C07D213-79
ICS C07D213-81; C07D213-89; A61K031-44; A61P011-00; A61P019-00;
A61P025-00; A61P029-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

IT 284461-74-1P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-carbamoyl(4-pyridyloxy)phenyl]urea 284462-18-6P
583840-03-3P 583840-04-4P 583840-09-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aryl ureas for therapeutic use as kinase inhibitors)

IT 583840-05-5P 583840-06-6P 583840-07-7P
583840-08-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl ureas for therapeutic use as kinase inhibitors)

IT 99586-65-9P, 4-Chloro-2-pyridinecarboxamide 284461-73-0P,
N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)(4-pyridyloxy)phenyl]urea 284462-80-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aryl ureas for therapeutic use as kinase inhibitors)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 39 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:656581 HCAPLUS Full-text
DOCUMENT NUMBER: 139:197370
TITLE: Preparation of aryl ureas containing pyridine, quinoline and isoquinoline N-oxide functionality as kinase inhibitors
INVENTOR(S): Dumas, Jacques; Scott, William J.; Riedl, Bernd
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

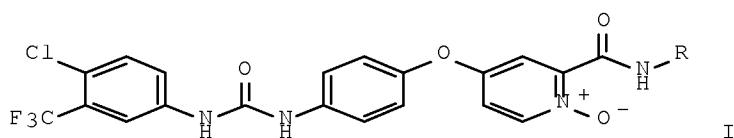
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|--------------|
| WO 2003068229 | A1 | 20030821 | WO 2003-US4110 | 20030211 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, | | | | |

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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|------------------------|----|----------|-----------------|-----------------|
| AU 2003209119 | A1 | 20030904 | AU 2003-209119 | 20030211 <-- |
| US 20030216396 | A1 | 20031120 | US 2003-361850 | 20030211 <-- |
| US 20070265315 | A1 | 20071115 | US 2007-775457 | 20070710 <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-354935P | P 20020211 <-- |
| | | | US 2003-361850 | B1 20030211 <-- |
| | | | WO 2003-US4110 | W 20030211 <-- |

OTHER SOURCE(S): MARPAT 139:197370
 GI



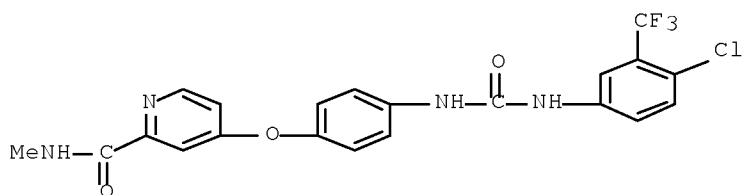
AB The title ureas containing a pyridine, quinoline, or isoquinoline functionality which is oxidized at the nitrogen heteroatom MLBNHCONHA [A = (un)substituted Ph, naphthyl, 5-6 membered monocyclic heteroaryl, 8-10 membered bicyclic heteroaryl; B = (un)substituted phenylene, naphthylene, 5-6 membered monocyclic heteroarylene, 8-10 membered bicyclic heteroarylene; L = (CH₂)_mO(CH₂)_l, (CH₂)_m(CH₂)_l, (CH₂)_mCO(CH₂)_l, etc.; m, l = 0-4; M = (un)substituted pyridine-1-oxide, quinoline-1-oxide, isoquinoline-1-oxide; with the provisos] which are useful in the treatment of (i) raf mediated diseases, for example, cancer, (ii) p38 mediated diseases such as inflammation and osteoporosis, and (iii) VEGF mediated diseases such as angiogenesis disorders, were claimed. Preparation of two ureas such as I [R = H, Me] which are not compds. of the invention, and have been distinguished from the compds. of the invention by a proviso, was described. Pharmaceutical composition comprising the title ureas was claimed.

IT 284461-73-0

RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of aryl ureas containing pyridine, quinoline and isoquinoline N-oxide functionality as kinase inhibitors)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c
 arboxyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K031-44
 ICS A61K031-47; C07D213-89; C07D215-60; C07D217-08; A61P035-00;
 A61P029-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1, 63

IT 123-30-8, 4-Aminophenol 320-51-4 176977-85-8, Methyl
 4-chloro-2-pyridinecarboxylate hydrochloride 284461-73-0
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of aryl ureas containing pyridine, quinoline and isoquinoline
 N-oxide functionality as kinase inhibitors)

IT 99586-65-9P 284461-74-1P 284462-80-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of aryl ureas containing pyridine, quinoline and isoquinoline
 N-oxide functionality as kinase inhibitors)

IT 583840-03-3P 583840-04-4P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of aryl ureas containing pyridine, quinoline and isoquinoline
 N-oxide functionality as kinase inhibitors)

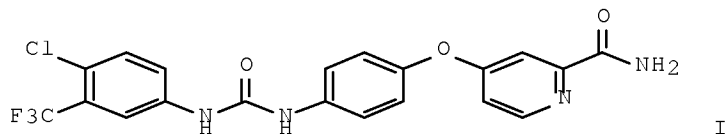
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 40 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2003:656580 HCAPLUS Full-text
 DOCUMENT NUMBER: 139:197369
 TITLE: Preparation of aryl ureas with angiogenesis inhibiting
 activity
 INVENTOR(S): Dumas, Jacques; Scott, William J.; Elting, James;
 Hatoum-Makdad, Holia
 PATENT ASSIGNEE(S): Bayer Corporation, USA
 SOURCE: PCT Int. Appl., 83 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------|--|----------|-----------------|--------------|
| WO 2003068228 | A1 | 20030821 | WO 2003-US4103 | 20030211 <-- |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2475703 | A1 | 20030821 | CA 2003-2475703 | 20030211 <-- |
| AU 2003209116 | A1 | 20030904 | AU 2003-209116 | 20030211 <-- |
| US 20030207870 | A1 | 20031106 | US 2003-361858 | 20030211 <-- |
| EP 1478358 | A1 | 20041124 | EP 2003-707846 | 20030211 <-- |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| JP 2005522448 | T | 20050728 | JP 2003-567410 | 20030211 <-- |
| MX 2004PA07832 | A | 20050908 | MX 2004-PA7832 | 20040811 <-- |

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JP 2007302687 A 20071122 JP 2007-183948 20070713 <--
 PRIORITY APPLN. INFO.: US 2002-354950P P 20020211 <--
 JP 2003-567410 A3 20030211 <--
 WO 2003-US4103 W 20030211 <--
 OTHER SOURCE(S): MARPAT 139:197369
 GI

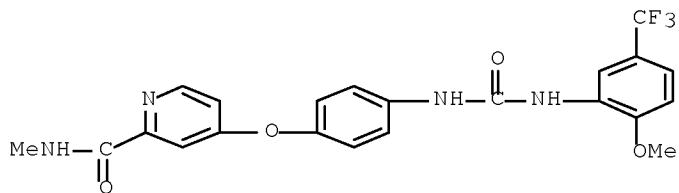


AB The title compds. ANHCONHB [A, B = (un)substituted Ph, naphthyl, 5-6 membered monocyclic heteroaryl, etc.], useful for treating diseases mediated by the VEGF induced signal transduction pathway characterized by abnormal angiogenesis or hyperpermeability processes, were claimed. Preps. of three title ureas are described. E.g., a 3-step synthesis of the urea I (starting from Me 4-chloro-2-pyridinecarboxylate hydrochloride), was given. The KDR (VEGFR2) assay for testing the title ureas is described.

IT 284461-44-5P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of aryl ureas with angiogenesis inhibiting activity)

RN 284461-44-5 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K031-44
 ICS A61K031-4436; A61K031-4725; A61K031-4709; A61K031-17; A61P035-00; A61P017-06; A61P019-02; A61P027-02

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1

IT 284461-44-5P 284461-73-0P 284461-74-1P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of aryl ureas with angiogenesis inhibiting activity)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/590724

L110 ANSWER 41 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:633416 HCAPLUS Full-text

DOCUMENT NUMBER: 139:173786

TITLE: Method for treating diseases associated with abnormal kinase activity

INVENTOR(S): Lyons, John; Rubinfeld, Joseph

PATENT ASSIGNEE(S): Supergen, Inc., USA

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-----------------|
| WO 2003065995 | A2 | 20030814 | WO 2003-US3537 | 20030206 <-- |
| WO 2003065995 | A3 | 20051013 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 20030147813 | A1 | 20030807 | US 2002-71849 | 20020207 <-- |
| US 20040127453 | A1 | 20040701 | US 2002-206854 | 20020726 <-- |
| US 6998391 | B2 | 20060214 | | |
| CA 2474174 | A1 | 20030814 | CA 2003-2474174 | 20030206 <-- |
| AU 2003215065 | A1 | 20030902 | AU 2003-215065 | 20030206 <-- |
| EP 1572075 | A2 | 20050914 | EP 2003-710881 | 20030206 <-- |
| EP 1572075 | A3 | 20051207 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| PRIORITY APPLN. INFO.: | | | US 2002-71849 | A1 20020207 <-- |
| | | | US 2002-206854 | A1 20020726 <-- |
| | | | WO 2003-US3537 | W 20030206 <-- |

AB Methods are provided for treating diseases associated with abnormal activity of kinases such as chronic myelogenous leukemia. The method comprises: administering a DNA methylation inhibitor to the patient in therapeutically effective amount; and administering a kinase inhibitor such as imatinib mesylate to the patient in therapeutically effective amount, such that the in vivo activity of the kinase is reduced relative to that prior to the treatment. The method can be used to treat cancer associated with abnormal activity of kinases such as phosphatidylinositol 3'-kinase (PI3K), protein kinases including serine/threonine kinases such as Raf kinases, protein kinase kinases such as MEK, and tyrosine kinases such as those in the epidermal growth factor receptor family (EGFR), platelet-derived growth factor receptor family (PDGFR), vascular endothelial growth factor receptor (VEGFR) family, nerve growth factor receptor family (NGFR), fibroblast growth factor receptor family (FGFR) insulin receptor family, ephrin receptor family, Met family, Ror family, c-kit family, Src family, Fes family, JAK family, Fak family, Btk family, Syk/ZAP-70 family, and Abl family.

IT 284461-73-0, BAY 43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

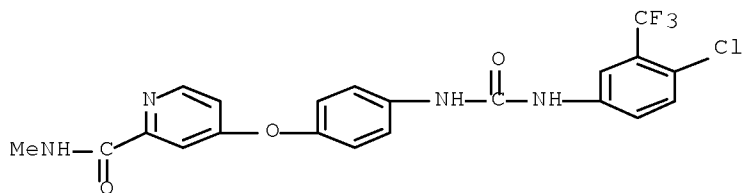
(treatment of diseases associated with abnormal kinase activity with

10/590724

serine/threonine kinase inhibitor and DNA methylation inhibitor)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c
arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K

CC 1-6 (Pharmacology)

IT 109511-58-2, U0126 154447-36-6, LY294002 167869-21-8, PD98059
212631-79-3, PD184352 284461-73-0, BAY 43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(treatment of diseases associated with abnormal kinase activity with
serine/threonine kinase inhibitor and DNA methylation inhibitor)

L110 ANSWER 42 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:454119 HCAPLUS Full-text

DOCUMENT NUMBER: 139:17567

TITLE: Aryl urea compounds in combination with other
cytostatic or cytotoxic agents for treating human
cancers and other raf kinase-mediated diseases

INVENTOR(S): Carter, Christopher A.; Dumas, Jacques; Gibson, Neil;
Hibner, Barbara; Humphrey, Rachel W.; Trail, Pamela;
Vincent, Patrick W.; Zhai, Yifan; Riedl, Bernd; Khire,
Uday; Lowinger, Timothy B.; Scott, William J.; Smith,
Roger A.; Wood, Jill E.; Monahan, Mary-Katherine;
Natero, Reina; Renick, Joel; Sibley, Robert N.

PATENT ASSIGNEE(S): Bayer Corporation, USA; Bayer AG

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|--------------|
| WO 2003047579 | A1 | 20030612 | WO 2002-US38439 | 20021203 <-- |
| <p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW</p> <p>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG</p> | | | | |

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| | | | | |
|---|----|----------|-----------------|-----------------|
| CA 2468463 | A1 | 20030612 | CA 2002-2468463 | 20021203 <-- |
| AU 2002351196 | A1 | 20030617 | AU 2002-351196 | 20021203 <-- |
| US 20030232765 | A1 | 20031218 | US 2002-308187 | 20021203 <-- |
| EP 1450799 | A1 | 20040901 | EP 2002-786842 | 20021203 <-- |
| EP 1450799 | B1 | 20061115 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| JP 2005511658 | T | 20050428 | JP 2003-548834 | 20021203 <-- |
| AT 345130 | T | 20061215 | AT 2002-786842 | 20021203 <-- |
| EP 1769795 | A2 | 20070404 | EP 2006-23696 | 20021203 <-- |
| EP 1769795 | A3 | 20080312 | | |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, SI, SK, TR, AL, LT, LV, MK, RO | | | | |
| ES 2275931 | T3 | 20070616 | ES 2002-786842 | 20021203 <-- |
| RU 2316326 | C2 | 20080210 | RU 2004-120785 | 20021203 <-- |
| IN 2004DN01420 | A | 20070316 | IN 2004-DN1420 | 20040526 <-- |
| MX 2004PA05137 | A | 20050603 | MX 2004-PA5137 | 20040528 <-- |
| ZA 2004004225 | A | 20050829 | ZA 2004-4225 | 20040528 <-- |
| US 20060247186 | A1 | 20061102 | US 2006-480360 | 20060705 <-- |
| PRIORITY APPLN. INFO.: | | | US 2001-334609P | P 20011203 <-- |
| | | | EP 2002-786842 | A3 20021203 <-- |
| | | | US 2002-308187 | B1 20021203 <-- |
| | | | WO 2002-US38439 | W 20021203 <-- |

OTHER SOURCE(S): MARPAT 139:17567

AB The invention discloses aryl urea compds. in combination with cytotoxic or cytostatic agents for use in treating raf kinase-mediated diseases, e.g. cancer.

IT 475207-59-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(aryl urea compds. in combination with other cytostatic or cytotoxic agents for treating human cancers and other raf kinase-mediated diseases)

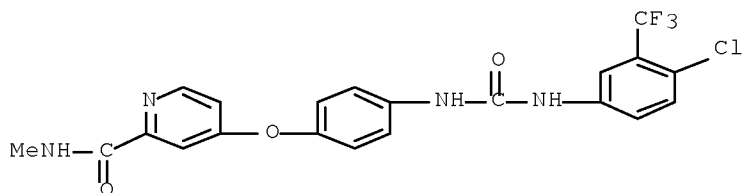
RN 475207-59-1 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl-, 4-methylbenzenesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 284461-73-0

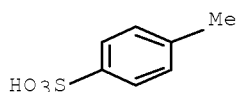
CMF C21 H16 Cl F3 N4 O3



CM 2

CRN 104-15-4

CMF C7 H8 O3 S



IC ICM A61K031-44
 ICS A61K031-535; A61K031-65; A61K031-435; A61K031-505; A61K031-47
 CC 1-6 (Pharmacology)
 IT 50-07-7, Mitomycin C 50-18-0, Cyclophosphamide 50-76-0, Actinomycin D
 51-21-8, 5-Fluorouracil 57-13-6D, Urea, aryl derivs. 57-22-7,
 Vincristine 59-05-2, Methotrexate 147-94-4, AraC 148-82-3, Melphalan
 154-93-8, BCNU 865-21-4, Vinblastine 4342-03-4, DTIC 5536-17-4, AraA
 13010-47-4, CCNU 15663-27-1, Cisplatin 23214-92-8, Doxorubicin
 25316-40-9, Doxorubicin hydrochloride 33069-62-4, Paclitaxel
 33419-42-0, Etoposide 41575-94-4, Carboplatin 71486-22-1, Vinorelbine
 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 114977-28-5, Taxotere
 122111-03-9, Gemzar 125317-39-7, Navelbine 180288-69-1, Herceptin
 184475-35-2, Gefitinib 475207-59-1
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (aryl urea compds. in combination with other cytostatic or cytotoxic
 agents for treating human cancers and other raf kinase-mediated
 diseases)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 43 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2003:454071 HCAPLUS Full-text
 DOCUMENT NUMBER: 139:30782
 TITLE: RAF-MEK-ERK pathway inhibitors to treat cancer
 INVENTOR(S): Lyons, John F.; Bollag, Gideon
 PATENT ASSIGNEE(S): Onyx Pharmaceuticals, Inc., USA
 SOURCE: PCT Int. Appl., 17 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|--------------|
| WO 2003047523 | A2 | 20030612 | WO 2002-US38402 | 20021203 <-- |
| WO 2003047523 | A3 | 20060223 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2466762 | A1 | 20030612 | CA 2002-2466762 | 20021203 <-- |
| AU 2002365899 | A1 | 20030617 | AU 2002-365899 | 20021203 <-- |

10/590724

AU 2002365899 B2 20070913
US 20030125359 A1 20030703 US 2002-308721 20021203 <--
US 7307071 B2 20071211
JP 2005526008 T 20050902 JP 2003-548784 20021203 <--
EP 1578346 A2 20050928 EP 2002-804478 20021203 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRIORITY APPLN. INFO.: US 2001-336886P P 20011204 <--
WO 2002-US38402 W 20021203 <--

AB Materials and methods for treating certain cancers are described, preferably cancers that result from the up-regulation of the RAF-MEK-ERK pathway, and more preferably chronic myelogenous leukemia, and which cancer is preferably resistant to the inhibitor of Bcr-Abl tyrosine kinase, imatinib.

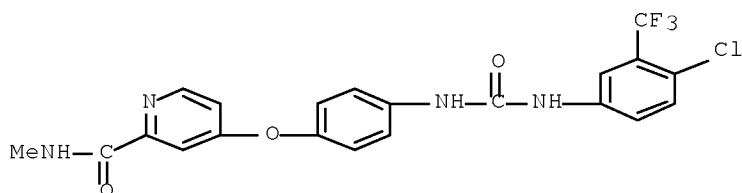
IT 284461-73-0, BAY 43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(BAY 43-9006; RAF-MEK-ERK pathway inhibitors to treat cancer)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c
arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K

CC 1-6 (Pharmacology)

IT 284461-73-0, BAY 43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(BAY 43-9006; RAF-MEK-ERK pathway inhibitors to treat cancer)

L110 ANSWER 44 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:173484 HCAPLUS Full-text

DOCUMENT NUMBER: 138:221581

TITLE: Method of using 5-(arylsulfonyl), 5-(arylsulfinyl) and
5-(arylsulfanyl)thiazolidine-2,4-diones for inhibition
of farnesyl-protein transferase

INVENTOR(S): Ayral-kaloustian, Semiramis; Epstein, Joseph William;
Birnberg, Gary Harold; Salaski, Edward James; Macewan,
Gloria Jean; Cheung, Katherine

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: PCT Int. Appl., 125 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

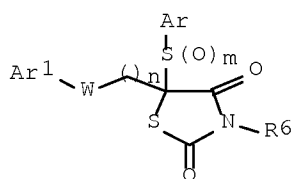
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

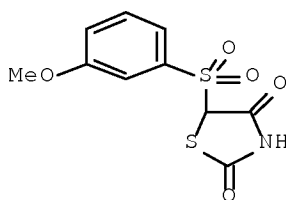
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|-------|-----------------|-------|
| ----- | ---- | ----- | ----- | ----- |

10/590724

WO 2003018135 A1 20030306 WO 2002-US26691 20020822 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG
AU 2002356135 A1 20030310 AU 2002-356135 20020822 <--
US 20030144301 A1 20030731 US 2002-226815 20020823 <--
US 6605628 B2 20030812
US 20030149063 A1 20030807 US 2002-227084 20020823 <--
US 6784184 B2 20040831
PRIORITY APPLN. INFO.: US 2001-314586P P 20010824 <--
US 2001-314621P P 20010824 <--
WO 2002-US26691 W 20020822 <--
OTHER SOURCE(S): MARPAT 138:221581
GI



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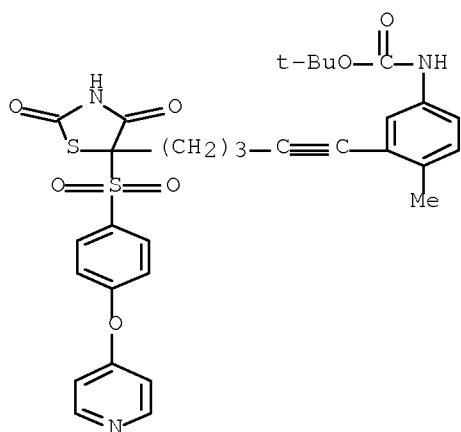


II

AB Title compds. I [Ar = naphthyl, quinolinyl, thienyl, pyridinyl, etc.; m = 0-2; R6 = H, alkyl, benzyl, etc.; W = C.tplbond.C, E/Z-CH=CH, CONH, etc.; n = 1-9; Ar1 = thienyl, pyridinyl, etc.] are prepared For instance, 5-bromothiazolidine-2,4-dione is reacted with 3-methoxybenzenethiol (THF, NaHMDS, -78°-room temperature); the intermediate sulfanyl derivative is oxidized (HOAc, H2O2) to give II. I are inhibitors of Ras FPTase, and may be used as an alternative to, or in conjunction with, traditional cancer therapy for treating ras-oncogene-dependent tumors, such as cancers of the pancreas, colon, bladder, and thyroid.

IT 500710-93-0P, tert-Butyl [3-[5-[2,4-dioxo-5-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of using 5-(arylsulfonyl), 5-(arylsulfinyl) and 5-(arylsulfanyl)thiazolidine-2,4-diones for inhibition of farnesyl-protein transferase)

RN 500710-93-0 HCAPLUS
CN Carbamic acid, [3-[5-[2,4-dioxo-5-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-5-thiazolidinyl]-1-pentynyl]-4-methylphenyl]-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)



IC ICM A61P035-00
 CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1, 63
 IT 125518-56-1P, 5-(4-Fluorophenylsulfonyl)thiazolidine-2,4-dione
 125540-45-6P 173019-14-2P, 5-[3-(4-Chlorophenyl)-2-propynyl]-5-[(4-methylphenyl)sulfonyl]thiazolidine-2,4-dione 173019-20-0P,
 5-[3-(4-Chlorophenyl)prop-2-ynyl]-5-(4-fluorobenzenesulfonyl)thiazolidine-2,4-dione 173019-22-2P, 5-[3-(4-Chlorophenyl)prop-2-ynyl]-5-(naphthalene-2-sulfonyl)thiazolidine-2,4-dione 173019-23-3P, 5-Benzenesulfonyl-5-[3-(4-chlorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-24-4P,
 5-Benzenesulfonyl-5-(3-phenylprop-2-ynyl)thiazolidine-2,4-dione 173019-26-6P, 5-(4-Chlorobenzenesulfonyl)-5-(3-phenylprop-2-ynyl)thiazolidine-2,4-dione 173019-27-7P, 5-(4-Chlorobenzenesulfonyl)-5-[3-(4-chlorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-29-9P,
 5-(4-Bromobenzenesulfonyl)-5-[3-(4-chlorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-31-3P, 5-[3-(4-Fluorophenyl)prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 173019-33-5P,
 5-(4-Toluenesulfonyl)-5-[3-(p-tolyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-34-6P, 5-(4-Bromobenzenesulfonyl)-5-(3-phenylprop-2-ynyl)thiazolidine-2,4-dione 173019-36-8P, 5-(Naphthalene-2-sulfonyl)-5-(3-phenylprop-2-ynyl)thiazolidine-2,4-dione 173019-38-0P,
 5-(4-Toluenesulfonyl)-5-[3-(4-trifluoromethylphenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-40-4P, 5-[3-(4-Methoxyphenyl)prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 173019-41-5P,
 5-[3-(4-Bromophenyl)prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 173019-43-7P, 5-Benzenesulfonyl-5-[3-(4-trifluoromethylphenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-45-9P, 5-(4-Chlorobenzenesulfonyl)-5-[3-(4-fluorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-46-0P,
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 5-Benzenesulfonyl-5-[3-(2-chlorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-51-7P, 5-Benzenesulfonyl-5-[3-[3,5-bis(trifluoromethyl)phenyl]prop-2-ynyl]thiazolidine-2,4-dione 173019-52-8P, 5-[3-[3,5-Bis(trifluoromethyl)phenyl]prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 173019-53-9P, 5-Benzenesulfonyl-5-[3-(3-chlorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-56-2P, 5-(4-Fluorobenzenesulfonyl)-5-[3-(4-trifluoromethylphenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-62-0P, 5-[3-(4-Chlorophenyl)prop-2-ynyl]-5-(quinoline-2-

sulfonyl)thiazolidine-2,4-dione 204848-63-5P, 5-[3-(4-Chlorophenyl)prop-2-ynyl]-5-(p-tolylsulfanyl)thiazolidine-2,4-dione 204848-70-4P, 5-[3-(4-Bromophenyl)prop-2-ynyl]-5-(4-chlorobenzenesulfonyl)thiazolidine-2,4-dione 500708-44-1P, 5-(3-Methoxyphenylsulfonyl)thiazolidine-2,4-dione 500708-46-3P, 5-(4-Iodophenylsulfonyl)thiazolidine-2,4-dione 500708-48-5P, 5-((4-(Trifluoromethoxy)benzene)sulfonyl)thiazolidine-2,4-dione 500708-49-6P, 5-(3-Nitrobenzenesulfonyl)thiazolidine-2,4-dione 500708-54-3P, 5-(4-Nitrobenzenesulfonyl)thiazolidine-2,4-dione 500708-60-1P, 5-[[4-((Pyridin-4-yl)oxy)benzene]sulfonyl]thiazolidine-2,4-dione 500708-65-6P, 5-(4-Phenoxybenzenesulfonyl)thiazolidine-2,4-dione 500708-67-8P, 5-(4-Benzoyloxybenzenesulfonyl)thiazolidine-2,4-dione 500708-70-3P, 5-(3,4-Dimethoxybenzenesulfonyl)thiazolidine-2,4-dione 500708-73-6P, N-[5-((2,4-Dioxothiazolidine-5-yl)sulfonyl)-2-methoxyphenyl]acetamide 500708-78-1P, 5-(5-Chlorothiophene-2-sulfonyl)thiazolidine-2,4-dione 500708-81-6P, 5-(Thiophene-2-sulfonyl)thiazolidine-2,4-dione 500708-85-0P, 5-(5-(Pyridin-2-yl)thiophene-2-sulfonyl)thiazolidine-2,4-dione 500708-93-0P, 5-(4-Butoxybenzenesulfonyl)thiazolidine-2,4-dione 500709-00-2P, 500709-82-0P, 5-(4-Methoxyphenylsulfanyl)-5-(5-(thiophen-2-yl)pentan-4-ynyl)thiazolidine-2,4-dione 500709-83-1P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-fluorophenylsulfanyl)thiazolidine-2,4-dione 500709-85-3P, 5-[6-(4-Chlorophenyl)hexan-5-ynyl]-5-(4-methoxyphenylsulfanyl)thiazolidine-2,4-dione 500709-86-4P, 5-[11-(4-Chlorophenyl)undecan-10-ynyl]-5-(4-methoxyphenylsulfanyl)thiazolidine-2,4-dione 500709-87-5P, 5-[5-(2-Chlorophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500709-88-6P, 5-[5-(3-Chlorophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500709-90-0P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-iodobenzenesulfonyl)thiazolidine-2,4-dione 500709-91-1P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-fluorobenzenesulfonyl)thiazolidine-2,4-dione 500709-92-2P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-phenoxybenzenesulfonyl)thiazolidine-2,4-dione 500709-93-3P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(naphthalene-2-sulfonyl)thiazolidine-2,4-dione 500709-94-4P, N-[4-[[5-[5-(4-Chlorophenyl)pentan-4-ynyl]-2,4-dioxothiazolidine-5-yl]sulfonyl]phenyl]acetamide 500709-95-5P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(quinoline-8-sulfonyl)thiazolidine-2,4-dione 500709-96-6P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-nitrobenzenesulfonyl)thiazolidine-2,4-dione 500709-97-7P, 5-(4-Benzoyloxybenzenesulfonyl)-5-[5-(4-chlorophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500709-98-8P, 5-(4-Butoxybenzenesulfonyl)-5-[5-(4-chlorophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500709-99-9P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(naphthalene-1-sulfonyl)thiazolidine-2,4-dione 500710-01-0P, 5-[5-(2,5-Dichlorophenyl)pentan-4-ynyl]-5-(4-iodobenzenesulfonyl)thiazolidine-2,4-dione 500710-02-1P 500710-03-2P, 5-[5-(2,4-Dichlorophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-05-4P, 5-[5-(3-Nitrophenyl)pentan-4-ynyl]-5-(4-phenoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-06-5P, 5-(4-Iodobenzenesulfonyl)-5-[5-(4-nitrophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-07-6P, 5-(4-Methoxybenzenesulfonyl)-5-[5-(4-nitrophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-08-7P, 5-(4-Methoxybenzenesulfonyl)-5-[5-(2-methyl-5-nitrophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-09-8P 500710-10-1P, 5-[5-(2-Methyl-5-nitrophenyl)pentan-4-ynyl]-5-(4-phenoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-11-2P, 5-(4-Iodobenzenesulfonyl)-5-[5-(2-methyl-5-nitrophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-12-3P, 5-[5-(2-Methyl-5-nitrophenyl)pentan-4-ynyl]-5-(naphthalene-1-sulfonyl)thiazolidine-2,4-dione 500710-13-4P, 5-[5-(2-Methyl-5-nitrophenyl)pentan-4-ynyl]-5-(naphthalene-2-sulfonyl)thiazolidine-2,4-dione 500710-14-5P, 5-[5-(2-Methyl-4-nitrophenyl)pentan-4-ynyl]-5-[[4-((pyridin-4-

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 4-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-
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 5-(4-Methoxybenzenesulfonyl)-5-[5-(4-(pyrrol-1-yl)phenyl)pentan-4-
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 (4-(pyrrol-1-yl)phenyl)pentan-4-ynyl]thiazolidine-2,4-dione
 500710-49-6P, 5-[5-(4-(Pyrrol-1-yl)phenyl)pentan-4-ynyl]-5-((4-
 trifluoromethoxybenzene)sulfonyl)thiazolidine-2,4-dione 500710-50-9P,
 5-(3-Methoxybenzenesulfonyl)-5-(5-(thiophen-2-yl)pentan-4-
 ynyl)thiazolidine-2,4-dione 500710-51-0P, 5-(4-Methylphenylsulfonyl)-5-
 (5-(thiophen-2-yl)pentan-4-ynyl)thiazolidine-2,4-dione 500710-52-1P,
 5-(4-Methoxybenzenesulfonyl)-5-(5-(thiophen-2-yl)pentan-4-
 ynyl)thiazolidine-2,4-dione 500710-53-2P, 5-(4-Methoxybenzenesulfonyl)-5-
 (3-(pyridin-3-yl)prop-2-ynyl)thiazolidine-2,4-dione 500710-54-3P,
 5-(3-(Thiophen-2-yl)prop-2-ynyl)-5-(toluene-4-sulfonyl)thiazolidine-2,4-
 dione 500710-55-4P, 5-(3-(1,1'-Biphenyl-4-yl)prop-2-ynyl)-5-(4-
 toluenesulfonyl)thiazolidine-2,4-dione 500710-56-5P,
 5-[3-(4-Phenoxyphenyl)prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-
 dione 500710-57-6P, 5-(3-(1,1'-Biphenyl-4-yl)prop-2-ynyl)-5-(4-
 methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-59-8P,
 5-(5-(Pyridin-3-yl)pentan-4-ynyl)-5-(4-toluenesulfonyl)thiazolidine-2,4-
 dione 500710-60-1P, 5-[5-(5-Amino-2-methylphenyl)pentan-4-ynyl]-5-(4-

methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-61-2P,
 [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid Benzyl Ester 500710-62-3P 500710-63-4P,
 [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid 4-chlorophenyl Ester 500710-64-5P,
 [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid Methyl Ester 500710-65-6P,
 [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid isopropyl Ester 500710-66-7P,
 [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid Neopentyl Ester 500710-67-8P,
 [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid Butyl Ester 500710-68-9P 500710-69-0P,
 N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]-2-methylpropanamide 500710-70-3P,
 N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]-3,3-dimethylbutanamide 500710-71-4P,
 N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]-2,2-dimethylpropanamide 500710-72-5P,
 N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]-2-phenylacetamide 500710-73-6P,
 N-Benzyl-N'-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]urea 500710-74-7P, N-(4-Methoxyphenyl)-N'-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]urea 500710-75-8P, N-(4-Chlorophenyl)-N'-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]urea 500710-76-9P, N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]-N'-(4-methylphenyl)urea 500710-77-0P, 4-Chloro-N-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]benzamide 500710-78-1P, 4-Methoxy-N-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]benzamide 500710-79-2P, N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl][1,1'-biphenyl]-4-carboxamide 500710-80-5P,
 4-(tert-Butyl)-N-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]benzamide 500710-81-6P,
 5-[5-(4-Chlorophenyl)-4-pentynyl]-5-[(5-chloro-2-thienyl)sulfonyl]-1,3-thiazolidine-2,4-dione 500710-82-7P, 5-[5-(4-Chlorophenyl)-4-pentynyl]-5-(2-thienylsulfonyl)-1,3-thiazolidine-2,4-dione 500710-83-8P,
 5-[5-(4-Chlorophenyl)-4-pentynyl]-5-[(3,4-dimethoxyphenyl)sulfonyl]-1,3-thiazolidine-2,4-dione 500710-84-9P, 5-[5-(4-Chlorophenyl)-4-pentynyl]-5-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-1,3-thiazolidine-2,4-dione 500710-85-0P, 5-[5-(4-Chlorophenyl)-4-pentynyl]-5-[[5-(2-pyridinyl)-2-thienyl]sulfonyl]-1,3-thiazolidine-2,4-dione 500710-86-1P,
 5-[(5-Chloro-2-thienyl)sulfonyl]-5-[5-(2,5-dichlorophenyl)-4-pentynyl]-1,3-thiazolidine-2,4-dione 500710-87-2P, 5-[5-(2,5-Dichlorophenyl)-4-pentynyl]-5-(2-thienylsulfonyl)-1,3-thiazolidine-2,4-dione 500710-88-3P, 5-[5-(2,5-Dichlorophenyl)-4-pentynyl]-5-[(3,4-dimethoxyphenyl)sulfonyl]-1,3-thiazolidine-2,4-dione 500710-89-4P, 5-[5-(2,5-Dichlorophenyl)-4-pentynyl]-5-[[5-(2-pyridinyl)-2-thienyl]sulfonyl]-1,3-thiazolidine-2,4-dione 500710-90-7P, [3-[5-[5-[(5-Chloro-2-thienyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamic acid tert-butyl ester 500710-91-8P, tert-Butyl [3-[5-[2,4-dioxo-5-(2-thienylsulfonyl)-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamate 500710-92-9P, tert-Butyl [3-[5-[5-[(3,4-dimethoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamate 500710-93-0P, tert-Butyl [3-[5-[2,4-dioxo-5-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamate 500710-94-1P, tert-Butyl [3-[5-[2,4-dioxo-5-[[5-

(2-pyridinyl)-2-thienyl)sulfonyl]-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamate 500710-95-2P, N-(tert-Butyl)-3-[5-[5-[(5-chloro-2-thienyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylbenzamide 500710-96-3P, N-(tert-Butyl)-3-[5-[2,4-dioxo-5-(2-thienyl)sulfonyl]-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylbenzamide 500710-97-4P, N-(tert-Butyl)-3-(5-[5-[(3,4-dimethoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl)-4-methylbenzamide 500710-98-5P, N-(tert-Butyl)-3-[5-[2,4-dioxo-5-[[5-(2-pyridinyl)-2-thienyl)sulfonyl]-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylbenzamide 500710-99-6P, 4-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-3-methylbenzoic Acid 500711-00-2P, N-(4-Chlorobenzyl)-3-[5-(4-methoxyphenyl)sulfonyl]-2,4-dioxothiazolidin-5-yl]propionamide 500711-02-4P, N-[2-(4-Chlorophenyl)ethyl]-3-[5-(4-methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]propionamide 500711-03-5P, 5-[(4Z)-5-(4-Chlorophenyl)pent-4-enyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500711-04-6P 500711-08-0P, 5-[3-(4-Chlorophenyl)propyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500711-09-1P, 5-[5-(3-Aminophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500711-10-4P, 5-(3-Phenylprop-2-enyl)-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500711-11-5P 500711-12-6P 500711-13-7P, 5-(4-Methoxyphenyl)sulfinyl]thiazolidine-2,4-dione 500711-14-8P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-methoxyphenyl)sulfinyl]thiazolidine-2,4-dione 500711-15-9P, Benzyl 5-[5-[5-[(benzyloxy)carbonyl]amino]-2-methylphenyl]pentan-4-ynyl]-5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-16-0P, 4-Nitrobenzyl 5-[(4-methoxyphenyl)sulfonyl]-5-[5-[2-methyl-5-[[[(4-nitrobenzyl)oxy]carbonyl]amino]phenyl]pentan-4-ynyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-17-1P, Methyl 5-[5-[5-[(methoxycarbonyl)amino]-2-methylphenyl]pentan-4-ynyl]-5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-18-2P, Isopropyl 5-[5-[5-[(isopropoxycarbonyl)amino]-2-methylphenyl]pentan-4-ynyl]-5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-19-3P 500711-20-6P, Butyl 5-[5-[5-[(butoxycarbonyl)amino]-2-methylphenyl]pentan-4-ynyl]-5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-21-7P, Isobutyl 5-[5-[5-[(isobutoxycarbonyl)amino]-2-methylphenyl]pentan-4-ynyl]-5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-22-8P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-3-(3-(imidazol-1-yl)propyl)-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500711-24-0P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)-3-methylthiazolidine-2,4-dione 500711-25-1P, 3-(2,4-Diethoxybenzyl)-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500711-26-2P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-3-(2,4-diethoxybenzyl)-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500711-28-4P, 5-[5-(2,5-Dichlorophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)-2,4-dioxothiazolidine-3-carboxylic acid 2-methoxyethyl ester 500711-31-9P, 5-[3-[3,5-Bis(trifluoromethyl)phenyl]prop-2-ynyl]thiazolidine-2,4-dione 500711-32-0P, [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pentan-1-ynyl-4-methylphenyl]carbamic acid neopentyl ester 500711-33-1P, N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]methyl]phenyl]-N'-(4-methylphenyl)urea

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(method of using 5-(arylsulfonyl), 5-(arylsulfinyl) and 5-(arylsulfanyl)thiazolidine-2,4-diones for inhibition of farnesyl-protein transferase)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 45 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2003:874965 HCAPLUS Full-text
 DOCUMENT NUMBER: 139:364958
 TITLE: Preparation of omega-carboxyaryl substituted diphenyl
 ureas as raf kinase inhibitors
 INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger,
 Timothy B.; Scott, William J.; Smith, Roger A.; Wood,
 Jill E.; Monahan, Mary-Katherine; Natero, Reina;
 Renick, Joel; Sibley, Robert N.
 PATENT ASSIGNEE(S): Bayer Corporation, USA
 SOURCE: U.S. Pat. Appl. Publ., 60 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|--------------|
| US 20030207872 | A1 | 20031106 | US 2002-42226 | 20020111 <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-42226 | 20020111 <-- |

OTHER SOURCE(S): MARPAT 139:364958

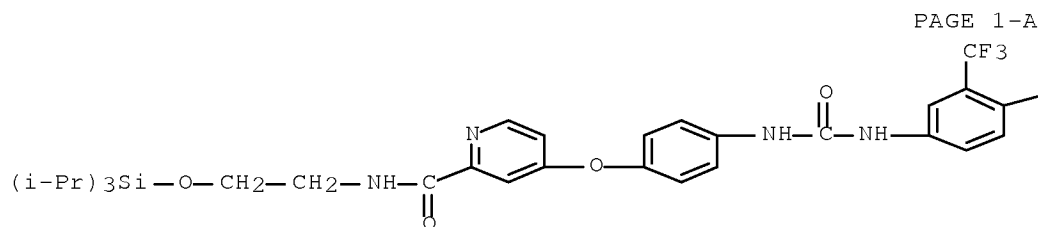
AB Urea derivs. of formula A-NHCONH-B or pharmaceutically acceptable salts thereof [A = a substituted moiety of up to 40 carbon atoms of the formula -L-(M-L1)q; where L = a 5 or 6 membered cyclic structure bound directly to D; L1 = a substituted cyclic moiety having at least 5 members; M = a bridging group having at least one atom; q = an integer of 1-3; each cyclic structure of L and L1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur; B = a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur] are prepared These compds. are useful for raf mediated diseases, in particular a cancerous cell growth mediated by raf kinase. All compds. exemplified, e.g. N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea, displayed IC50 of between 1 mM and 10 μ M.

IT 284462-06-2P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[[2-[N-(2-triisopropylsilyloxyethyl)carbamoyl]-4-pyridyl]oxy]phenyl]urea
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of ω -carboxyaryl substituted di-Ph ureas as raf kinase inhibitors for treating raf-mediated diseases such as cancerous cell growth)

RN 284462-06-2 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-[[tris(1-methylethyl)silyl]oxy]ethyl]- (CA INDEX NAME)



c1

IC ICM C07D417-02
 ICS C07D413-02; C07D043-02; C07D041-02; A61K031-541; A61K031-5377;
 A61K031-496; A61K031-4545; A61K031-454; A61K031-427

INCL 514227800; 514235500; 514252130; 514252140; 514253010; 514254010;
 514316000; 514326000; 514365000; 514397000

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1, 7, 27

IT 349-65-5P, 2-Methoxy-5-(trifluoromethyl)aniline 703-12-8P,
 N-Methyl-4-bromobenzenesulfonamide 883-62-5P, 3-Methoxy-2-naphthoic Acid
 1215-98-1P, 4-(4-Acetylphenoxy)aniline 13041-60-6P, Methyl
 3-methoxy-2-naphthoate 16588-75-3P, 2-Methoxy-5-(trifluoromethyl)phenyl
 isocyanate 27237-21-4P, 4-(3-Carboxyphenoxy)-1-nitrobenzene
 36089-89-1P, 4-(4-Methylsulfonylphenoxy)-1-nitrobenzene 41513-02-4P,
 4-Bromo-3-(trifluoromethyl)phenyl Isocyanate 50727-06-5P,
 5-Hydroxyisoindoline-1,3-dione 51727-15-2P, 4-Chloropyridine-2-carbonyl
 chloride hydrochloride 53750-66-6P, 4-Chloropyridine-2-carbonyl chloride
 54579-63-4P, 4-(3-Carboxyphenoxy)aniline 64064-63-7P,
 4-(2-Methyl-5-pyridyloxy)-1-nitrobenzene 67291-63-8P,
 2-Amino-3-methoxynaphthalene 71708-64-0P, 4-[3-(N-
 Methylcarbamoyl)phenoxy]-1-nitrobenzene 73441-73-3P,
 4-[4-(N-Methylsulfamoyl)phenoxy]-1-nitrobenzene 73441-86-8P,
 4-[4-(N-Methylsulfamoyl)phenyloxy]aniline 75919-92-5P,
 4-(4-Acetylphenoxy)-1-nitrobenzene 77992-50-8P, 4-Bromo-3-
 (trifluoromethyl)aniline monohydrochloride 99586-65-9P,
 4-Chloro-2-pyridinecarboxamide 114780-06-2P, 4-Chloro-N,N-dimethyl-2-
 pyridinecarboxamide 119431-22-0P, 3-Chloro-4-(2,2,2-
 trifluoroacetyl amino)phenol 153435-79-1P, N-Methyl-3-
 bromobenzenesulfonamide 176977-85-8P, Methyl 4-chloropyridine-2-
 carboxylate hydrochloride 220000-87-3P, 4-Chloro-N-methyl-2-
 pyridinecarboxamide 228401-15-8P, 2-[N-(Carbobenzyloxy)amino]-3-
 methoxynaphthalene 228401-43-2P, 4-(3-Methoxycarbonyl-4-methoxyphenoxy)-
 1-nitrobenzene 228401-44-3P, 4-(3-Carboxy-4-methoxyphenoxy)-1-
 nitrobenzene 284461-86-5P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-
 [2-(methoxycarbonyl)-5-pyridyloxy]phenyl]urea 284462-06-2P,
 N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-[N-(2-
 triisopropylsilyloxyethyl)carbamoyl]-4-pyridyl]oxy]phenyl]urea
 284462-37-9P, 4-[2-(N-Methylcarbamyl)-4-pyridyloxy]aniline 284462-38-0P,
 5-(4-Nitrophenoxy)isoindoline-1,3-dione 284462-39-1P,
 5-(4-Aminophenoxy)isoindoline-1,3-dione 284462-40-4P,
 1-(4-tert-Butyl-2-nitrophenyl)-2,5-dimethylpyrrole 284462-41-5P,
 5-tert-Butyl-2-(2,5-dimethylpyrrolyl)aniline 284462-42-6P,
 4-[2-(N-Methylcarbamoyl)-4-pyridyloxy]-2-methylaniline hydrochloride
 284462-43-7P 284462-44-8P, 4-[2-(N-Methylcarbamoyl)-4-pyridyloxy]-2-
 chloroaniline 284462-45-9P, 4-Chloro-2-methoxy-5-
 (trifluoromethyl)aniline 284462-46-0P, 4-[3-(N-Methylcarbamoyl)-4-
 methoxyphenoxy]-1-nitrobenzene 284462-47-1P, 4-[3-(N-Methylcarbamoyl)-4-
 methoxyphenoxy]aniline 284462-48-2P, 5-(4-Nitrophenoxy)-2-
 methylisoindoline-1,3-dione 284462-49-3P, 5-(4-Aminophenoxy)-2-
 methylisoindoline-1,3-dione 284462-51-7P, 4-Chloro-2-[N-(2-morpholin-4-
 ylethyl)carbamoyl]pyridine 284462-52-8P, 4-[2-[N-(2-Morpholin-4-

ylethyl)carbamoyl]-4-pyridyloxy]aniline 284462-53-9P,
 4-(1-Oxoisoindolin-5-yloxy)-1-nitrobenzene 284462-54-0P,
 4-(1-Oxoisoindolin-5-yloxy)aniline 284462-55-1P, 4-(3-Ethoxycarbonylphenoxy)-1-nitrobenzene 284462-56-2P, 4-[3-(N-Methylcarbamoyl)phenoxy]aniline 284462-57-3P, 4-(5-Methoxycarbonyl-3-pyridyloxy)-1-nitrobenzene 284462-58-4P, 4-(5-Methoxycarbonyl-3-pyridyloxy)aniline 284462-59-5P, 4-[3-(N-Methylsulfamoyl)phenyloxy]benzene 284462-60-8P, 4-[3-(N-Methylsulfamoyl)phenyloxy]-1-nitrobenzene 284462-61-9P, 4-(3-Methylsulfamoylphenoxy)aniline 284462-62-0P, 4-[4-[1-(Methoxyimino)ethyl]phenoxy]aniline hydrochloride 284462-63-1P, 4-Chloro-N-(2-triisopropylsilyloxy)ethylpyridine-2-carboxamide 284462-64-2P, 4-[[2-[N-(2-Triisopropylsilyloxyethyl)carbamoyl]-4-pyridyl]oxy]aniline 284462-65-3P, 4-(2-Methoxycarbonyl-5-pyridyloxy)-1-nitrobenzene 284462-66-4P, 4-(2-Methoxycarbonyl-5-pyridyloxy)aniline 284462-74-4P, 4-[2-(N-Methylcarbamoyl)-4-pyridyloxy]-2-methylaniline 284462-77-7P, 5-tert-Butyl-2-methoxyphenyl isocyanate 284462-78-8P, 3-[-2-(N-Methylcarbamoyl)-4-pyridyloxy]aniline 284462-79-9P, 3-(2-Carbamoyl-4-pyridyloxy)aniline 284462-80-2P, 4-(2-Carbamoyl-4-pyridyloxy)aniline 284462-82-4P, 4-[2-(N-Ethylcarbamoyl)-4-pyridyloxy]aniline 284462-83-5P, 4-[2-(N-Methylcarbamoyl)-4-pyridyloxy]-3-chloroaniline 284462-84-6P 284462-85-7P, 4-(3-Carbamoylphenoxy)aniline 284462-86-8P, 4-[2-(N,N-Dimethylcarbamoyl)-4-pyridyloxy]aniline 284462-89-1P, 4-[2-(N-Isopropylcarbamoyl)-4-pyridyloxy]aniline 284462-92-6P, 3-[2-(N-Methylcarbamoyl)-4-pyridyloxy]-4-methylaniline 284462-93-7P, 4-[3-[N-(2-Morpholinylethyl)carbamoyl]phenoxy]aniline 284462-94-8P, 4-[3-[N-(2-Piperidylethyl)carbamoyl]phenoxy]aniline 284462-95-9P, 4-[3-[N-(Tetrahydrofurylmethyl)carbamoyl]phenoxy]aniline 284462-99-3P, 4-Chloro-2-methoxy-5-(trifluoromethyl)phenyl isocyanate 284670-99-1P, 4-(4-Acetylphenoxy)-5-aminopyridine 284671-00-7P, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-[4-[3-(5-methoxycarbonylpyridyl)oxy]phenyl]urea 284671-01-8P, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-(3-carboxyphenyl)urea 573673-51-5P, 4-[4-[2-(N-Methylcarbamoyl)phenyl]thio]aniline 573673-52-6P, 3-[4-[2-(N-Methylcarbamoyl)phenyl]thio]aniline 573673-55-9P, 4-[3-[N-[(1-Methyl-2-pyrrolidinyl)methyl]carbamoyl]phenoxy]aniline 604813-03-8P, 4-(5-Methylcarbamoyl-3-pyridyloxy)aniline 604813-05-0P 604813-07-2P, 4-Chloro-N-ethyl-2-pyridinecarboxamide 604813-08-3P, 4-Chloro-N-isopropyl-2-pyridinecarboxamide 604813-09-4P, 4-[4-(N-Methylsulfamoyl)phenoxy]benzene 604813-11-8P, 4-[3-[N-(2-Morpholinylethyl)carbamoyl]phenoxy]-1-nitrobenzene 604813-12-9P, 4-[3-[N-(2-Piperidylethyl)carbamoyl]phenoxy]-1-nitrobenzene 604813-13-0P, 4-[3-[N-(Tetrahydrofurylmethyl)carbamoyl]phenoxy]-1-nitrobenzene 604813-14-1P, 4-[3-[N-[(1-Methyl-2-pyrrolidinyl)methyl]carbamoyl]phenoxy]-1-nitrobenzene
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of ω-carboxyaryl substituted di-Ph ureas as raf kinase inhibitors for treating raf-mediated diseases such as cancerous cell growth)

| | | | | | |
|----|--------------|--------------|--------------|--------------|--------------|
| IT | 228418-48-2P | 284461-33-2P | 284461-34-3P | 284461-35-4P | 284461-36-5P |
| | 284461-37-6P | 284461-38-7P | 284461-39-8P | 284461-40-1P | 284461-41-2P |
| | 284461-42-3P | 284461-43-4P | 284461-44-5P | | |
| | 284461-45-6P | 284461-46-7P | 284461-47-8P | | |
| | 284461-48-9P | 284461-49-0P | 284461-50-3P | | |
| | 284461-51-4P | 284461-52-5P | 284461-53-6P | 284461-54-7P | |
| | 284461-55-8P | 284461-56-9P | 284461-57-0P | 284461-58-1P | |
| | 284461-59-2P | 284461-60-5P | 284461-61-6P | 284461-62-7P | |
| | 284461-63-8P | 284461-64-9P | 284461-65-0P | 284461-66-1P | 284461-67-2P |
| | 284461-68-3P | 284461-70-7P | 284461-71-8P | 284461-72-9P | |
| | 284461-73-0P | 284461-74-1P | 284461-75-2P | | |

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284461-76-3P 284461-77-4P 284461-78-5P 284461-79-6P
284461-80-9P 284461-81-0P 284461-82-1P
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284461-93-4P 284461-94-5P 284461-95-6P 284461-96-7P 284461-97-8P
284461-99-0P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(3-methylcarbamoylphenyl)carbamoylphenyl]urea 284462-00-6P 284462-01-7P
284462-02-8P 284462-03-9P 284462-04-0P 284462-05-1P
284462-07-3P 284462-08-4P 284462-09-5P 284462-10-8P 284462-11-9P
284462-12-0P 284462-13-1P 284462-15-3P 284462-16-4P
284462-17-5P 284462-18-6P 284462-19-7P
284462-20-0P 284462-21-1P 284462-22-2P
284462-23-3P 284462-24-4P 284462-25-5P 284462-26-6P
284462-27-7P 284462-28-8P 284462-29-9P
284462-30-2P 284462-31-3P 284462-34-6P
284462-35-7P, N-[5-(tert-Butyl)-2-(2,5-dimethylpyrrolyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284462-36-8P
284462-70-0P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[N-[3-[N-(3-pyridyl)carbamoyl]phenyl]carbamoyl]phenyl]urea 284670-98-0P,
N,N'-Bis[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 447457-08-1P
573673-43-5P 604813-02-7P 604813-04-9P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[3-[5-(2-dimethylaminoethyl)carbamoyl]pyridyl]oxy]phenyl]urea 620962-97-2P 620962-98-3P
620962-99-4P 620963-00-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of ω -carboxyaryl substituted di-Ph ureas as raf kinase inhibitors for treating raf-mediated diseases such as cancerous cell growth)

L110 ANSWER 46 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:590832 HCAPLUS Full-text

DOCUMENT NUMBER: 139:149528

TITLE: Preparation of diphenylureas as RAF kinase inhibitors

INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 62 pp., Cont. of U. S. Ser. No. 42,203.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

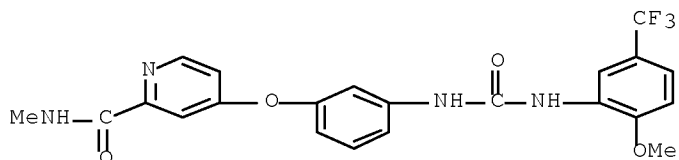
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-----------------|
| US 20030144278 | A1 | 20030731 | US 2002-283248 | 20021030 <-- |
| US 7235576 | B1 | 20070626 | US 2002-42203 | 20020111 <-- |
| PRIORITY APPLN. INFO.: | | | US 2001-367380P | P 20010112 <-- |
| | | | US 2002-42203 | A1 20020111 <-- |

OTHER SOURCE(S): MARPAT 139:149528

AB ADB [I; D = NHCONH; A = L(ML1)q; L = 5-6 membered cyclic structure bound directly to D; L1 = substituted cyclic moiety having ≥ 5 members, M = bridging group having ≥ 1 atom; q = 1-3; L, L1 contain 0-4 N, O, S; B = (substituted) up to tricyclic aryl, heteroaryl of ≤ 30 C atoms with ≥ 1 6-membered cyclic

structure bound directly to D containing 0-4 N, O, S], were prepared Thus, 4-chloro-3-(trifluoromethyl)phenyl isocyanate in CH₂Cl₂ was added dropwise to a suspension of 4-[2-(N-methylcarbamoyl)-4-pyridyloxy]aniline (preparation given) in CH₂Cl₂ at 0°; the resulting mixture was stirred at room temperature for 22 h. to afford N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea. I inhibited RAF kinase in the range 1 nM-1 μM. I pharmaceutical compns. are claimed.

IT 284461-42-3P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of diphenylureas as RAF kinase inhibitors)
 RN 284461-42-3 HCAPLUS
 CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K031-541
 ICS A61K031-5377; A61K031-496; A61K031-454; A61K031-4025; C07D417-02; C07D413-02; C07D043-02
 INCL 514227800; 514231500; 514252130; 514326000; 514422000; 544060000; 544111000; 544359000; 546207000
 CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1, 25, 63
 IT 228418-48-2P 284461-33-2P, N-(3-tert-Butylphenyl)-N'-[4-[3-(N-methylcarbamoyl)phenoxy]phenyl] urea 284461-34-3P, N-(3-tert-Butylphenyl)-N'-[4-(4-acetylphenoxy)phenyl] urea 284461-35-4P 284461-36-5P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-[3-(N-methylcarbamoyl)phenoxy]phenyl]urea 284461-37-6P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-[4-methoxy-3-(N-methylcarbamoyl)phenoxy]phenyl]urea 284461-38-7P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-(1,3-dioxoisindolin-5-yloxy)phenyl]urea 284461-39-8P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-(1-oxoisindolin-5-yloxy)phenyl] urea 284461-40-1P 284461-41-2P 284461-42-3P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea 284461-43-4P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl] urea 284461-44-5P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea 284461-45-6P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridyloxy)phenyl] urea 284461-46-7P 284461-47-8P 284461-48-9P 284461-49-0P 284461-50-3P 284461-51-4P 284461-52-5P 284461-53-6P 284461-54-7P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-(1,3-dioxoisindolin-5-yloxy)phenyl] Urea 284461-55-8P 284461-56-9P 284461-57-0P 284461-58-1P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridylthio]phenyl] urea 284461-59-2P 284461-60-5P 284461-61-6P 284461-62-7P 284461-63-8P 284461-64-9P

284461-65-0P 284461-66-1P 284461-67-2P 284461-68-3P 284461-69-4P
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 N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284461-74-1P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridyloxy)phenyl]urea 284461-75-2P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl] urea 284461-76-3P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284461-77-4P 284461-78-5P
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 284462-25-5P 284462-26-6P 284462-27-7P 284462-28-8P,
 N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea 284462-29-9P
 284462-30-2P 284462-31-3P, N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea 284462-32-4P 284462-34-6P 284462-35-7P
 284462-67-5P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(4-aminophenyl) Urea 284462-68-6P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(4-ethoxycarbonylphenyl)urea 284462-70-0P 284462-97-1P 284670-98-0P
 447457-08-1P 447457-09-2P 474642-51-8P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(3-carboxyphenyl)urea 474642-55-2P
 573673-42-4P 573673-43-5P 573673-45-7P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diphenylureas as RAF kinase inhibitors)

IT 98-98-6, Picolinic acid 100-51-6, Benzyl alcohol, reactions 106-50-3, p-Phenylenediamine, reactions 108-00-9 109-85-3 110-13-4, Acetylacetone 110-91-8, Morpholine, reactions 123-30-8, 4-Aminophenol 123-39-7 320-51-4, 4-Chloro-3-trifluoromethylaniline 327-78-6, 4-Chloro-3-trifluoromethylphenyl isocyanate 349-65-5 350-46-9 393-36-2 462-08-8, 3-Pyridinamine 593-56-6, O-Methylhydroxylamine hydrochloride 610-35-5, 4-Hydroxyphthalic acid 619-08-9 626-61-9 883-99-8, Methyl 3-hydroxy-2-naphthoate 1121-78-4 1215-98-1 1664-40-0 1877-71-0 2038-03-1, 4-Morpholineethanamine 2835-99-6, 4-Amino-3-methylphenol 2905-24-0 3535-88-4 5369-19-7 6310-19-6, 2-Nitro-4-tert-butylaniline 6628-77-9 6927-86-2 7781-98-8 16588-75-3 25900-61-2 29264-35-5 30766-22-4 30806-83-8 34803-66-2 36265-31-3 51639-48-6 73441-86-8 150009-83-9 256340-75-7 284461-86-5 284462-06-2 284462-44-8
 284462-71-1 284462-72-2 284462-73-3 284462-74-4 284462-76-6
 284462-77-7 284462-78-8 284462-79-9 284462-80-2 284462-82-4
 284462-84-6 284462-85-7 284462-86-8 284462-89-1 284462-92-6
 284462-93-7 284462-94-8 284462-95-9 284462-99-3 284670-99-1

284671-01-8 573673-48-0 573673-49-1 573673-50-4 573673-51-5
 573673-52-6 573673-53-7 573673-55-9 573673-56-0
 573673-58-2 573673-59-3 573673-60-6

RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of diphenylureas as RAF kinase inhibitors)

L110 ANSWER 47 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:123969 HCAPLUS Full-text

DOCUMENT NUMBER: 141:166948

TITLE: Raf pathway inhibitors in oncology

AUTHOR(S): Bollag, Gideon; Freeman, Scott; Lyons, John F.; Post, Leonard E.

CORPORATE SOURCE: Plexxikon Inc, Berkeley, CA, 94710, USA

SOURCE: Current Opinion in Investigational Drugs (Thomson Current Drugs) (2003), 4(12), 1436-1441
 CODEN: COIDAZ; ISSN: 1472-4472

PUBLISHER: Thomson Current Drugs

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Recognition of the importance of the Raf pathway in the proliferation and survival of tumor cells recently increased with the discovery of activating BRAF mutations in human tumors. Therefore, in addition to a role in controlling tumors with Ras mutations and activated growth factor receptors, inhibitors of the Raf pathway may harbor therapeutic potential in tumors carrying a BRAF oncogene. A variety of agents have been discovered that interfere with the Raf pathway, including antisense oligonucleotides and small mols. These inhibitors block the expression of Raf protein, block Ras/Raf interaction, block its kinase activity, or block the kinase activity of the Raf target protein mitogen-activated protein kinase kinase. Raf pathway inhibitors that are currently undergoing clin. evaluation show promising signs of anticancer efficacy with a very tolerable safety profile. Indeed, the Raf inhibitor BAY-43-9006 recently entered phase III clin. trials. Here, we review the current development status of potential Raf pathway therapeutics.

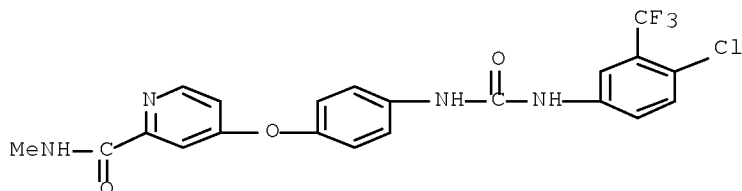
IT 284461-73-0, BAY-43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Raf pathway inhibitors were currently in clin. trial and showed promising anticancer efficacy with very tolerable safety profile and BAY-43-9006 recently entered phase III clin. trial)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-0 (Pharmacology)

IT 284461-73-0, BAY-43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(Raf pathway inhibitors were currently in clin. trial and showed promising anticancer efficacy with very tolerable safety profile and BAY-43-9006 recently entered phase III clin. trial)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 48 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:736198 HCAPLUS Full-text

DOCUMENT NUMBER: 139:301125

TITLE: BAY-43-9006 (Bayer/Onyx)

AUTHOR(S): Lee, John T.; McCubrey, James A.

CORPORATE SOURCE: Department of Microbiology and Immunology, Brody School of Medicine at East Carolina University, Greenville, NC, 27858-4353, USA

SOURCE: Current Opinion in Investigational Drugs (Thomson Current Drugs) (2003), 4(6), 757-763
CODEN: COIDAZ; ISSN: 1472-4472

PUBLISHER: Thomson Current Drugs

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

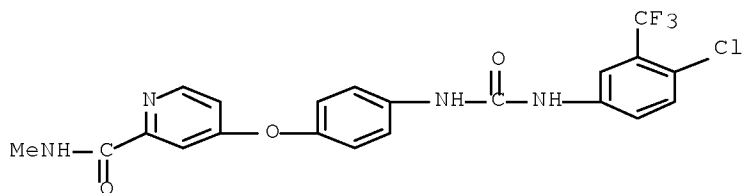
AB A review. Bayer and Onyx are developing BAY-43-9006, an oral cytostatic Raf kinase inhibitor for the potential treatment of colorectal and breast cancers, hepatocellular carcinoma and non-small-cell lung cancer, in addition to acute myelogenous leukemia, myelodysplastic syndrome and other cancers. A US IND was filed in May 2000 and by Feb. 2003 BAY-43-9006 was in phase II trials, with phase III trials expected to begin later in 2003.

IT 284461-73-0, BAY 43-9006

RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BAY 43-9006 for treatment of cancer patients)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-0 (Pharmacology)

IT 284461-73-0, BAY 43-9006

RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BAY 43-9006 for treatment of cancer patients)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 49 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:12708 HCAPLUS Full-text

DOCUMENT NUMBER: 140:70551
 TITLE: A Phase I clinical and pharmacokinetic study of the Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with doxorubicin in patients with solid tumors
 AUTHOR(S): Richly, H.; Kupsch, P.; Passage, K.; Grubert, M.; Hilger, R. A.; Kredtke, S.; Voliotis, D.; Scheulen, M. E.; Seeber, S.; Strumberg, D.
 CORPORATE SOURCE: West German Cancer Center, University of Essen, Essen, Germany
 SOURCE: International Journal of Clinical Pharmacology and Therapeutics (2003), 41(12), 620-621
 CODEN: ICTHEK; ISSN: 0946-1965
 PUBLISHER: Dustri-Verlag Dr. Karl Feistle
 DOCUMENT TYPE: Journal
 LANGUAGE: English

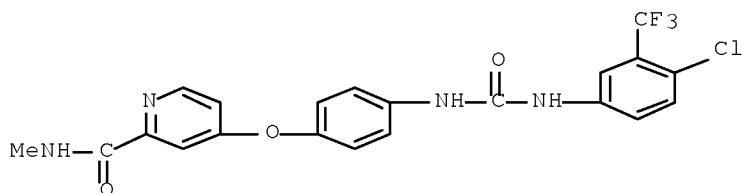
AB Objective: The primary objective of this phase I study was to define the safety profile of BAY 43-9006 administered in combination with doxorubicin. Patients and methods: Twenty-nine patients with advanced, refractory solid tumors were treated with doxorubicin (60mg/m²) every 3 wk for 6 consecutive cycles. BAY 43-9006 in combination with doxorubicin chemotherapy was administered at 3 dose levels. Results: Toxicity and response were evaluable in a total of 24 out of 29 enrolled patients. Dose-limiting toxicity was observed at various dose levels. Doxorubicin plasma C_{max}/AUC values increased on escalating the dose of BAY 43-9006. Patients with liver metastases and elevated values of AST and conjugated bilirubin, compared to patients with normal hepatic function, showed a higher AUC for doxorubicin at all dose levels. Conclusions: Our data suggest a pharmacol. interaction of BAY 43-9006 at DL 400 mg bid with doxorubicin resulting in significantly increased AUC for doxorubicin.

IT 284461-73-0, BAY 43-9006

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (clin. and pharmacokinetic study of Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with doxorubicin in patients with solid tumors)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-6 (Pharmacology)

IT 284461-73-0, BAY 43-9006

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (clin. and pharmacokinetic study of Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with doxorubicin in patients with solid tumors)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 50 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:12707 HCAPLUS Full-text

DOCUMENT NUMBER: 140:70550

TITLE: Drug-drug interaction pharmacokinetic study with the Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with irinotecan (CPT-11) in patients with solid tumors

AUTHOR(S): Mross, K.; Steinbild, S.; Baas, F.; Reil, M.; Buss, P.; Mersmann, S.; Voliotis, D.; Schwartz, B.; Brendel, E.

CORPORATE SOURCE: Tumor Biology Center at the Albert-Ludwigs-University Freiburg, Leverkusen, Germany

SOURCE: International Journal of Clinical Pharmacology and Therapeutics (2003), 41(12), 618-619

CODEN: ICTHEK; ISSN: 0946-1965

PUBLISHER: Dustri-Verlag Dr. Karl Feistle

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Classical cytotoxic anticancer drugs generally have specific actions but also interfere with signalling pathways. A logical approach is therefore to combine the Raf kinase inhibitor (RKI) with classical cytotoxic agents since recent work has shown that the RKI BAY 43-9006 and CPT-11 have additive or synergistic actions. Objective: Because a pharmacol. drug-drug interaction cannot be ruled out, interaction studies were started using the RKI BAY 43-9006 in combination with the most important anticancer drugs, such as CPT-11. Patients and methods: The study protocol included three groups of 6 patients with solid tumors given different RKI doses and the same dosage of CPT-11. Blood samples for measurement of CPT-11 and SN-38 were obtained both during and in the absence of RKI treatment. Results: Ests. of toxicity, response and pharmacokinetics during the first RKI dose could be made in a total of 9/18 patients. All symptoms of toxicity were considered to be due to CPT-11 or RKI. The PK evaluation showed no significant differences for CPT-11 and SN-38, with or without RKI. Conclusions: The combination CPT-11 and SN-38 PK is not significantly influenced by the addition of RKI. There is no indication that the PK of RKI are influenced significantly by CPT-11 and SN-38.

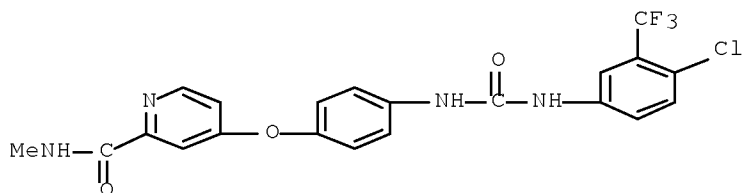
IT 284461-73-0, BAY 43-9006

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(drug-drug interaction pharmacokinetic study with Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with irinotecan (CPT-11) in patients with solid tumors)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-6 (Pharmacology)
 IT 284461-73-0, BAY 43-9006
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (drug-drug interaction pharmacokinetic study with Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with irinotecan (CPT-11) in patients with solid tumors)
 REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 51 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:12706 HCAPLUS Full-text

DOCUMENT NUMBER: 141:17009

TITLE: Antitumor effect and potentiation or reduction in cytotoxic drug activity in human colon carcinoma cells by the Raf kinase inhibitor (RKI) BAY 43-9006

AUTHOR(S): Heim, M.; Sharifi, M.; Hilger, R. A.; Scheulen, M. E.; Seeber, S.; Strumberg, D.

CORPORATE SOURCE: West German Cancer Center, University of Essen, Essen, Germany

SOURCE: International Journal of Clinical Pharmacology and Therapeutics (2003), 41(12), 616-617

CODEN: ICTHEK; ISSN: 0946-1965

PUBLISHER: Dustri-Verlag Dr. Karl Feistle

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A study was conducted to evaluate the effects of combining BAY 43-9006 and cytotoxic drugs (paclitaxel, 5-FU, oxaliplatin, and SN-38) on human cancer cells using 4 sequencing protocols and to analyze the effect of RKI on colorectal cancer cells showing marked resistance against SN-38. Results showed the additive action or moderate synergy using RKI in combination with numerous cytotoxic agents and the marked reduction of oxaliplatin activity by RKI in human carcinoma cells. These indicate that Raf kinase activity might be important for oxaliplatin-induced cytotoxicity. Furthermore, lacking cross-resistance between SN-38 and RKI might provide a rationale for designing clin. trials using CPT-11 in combination with BAY 43-9006 in patients with colorectal cancer.

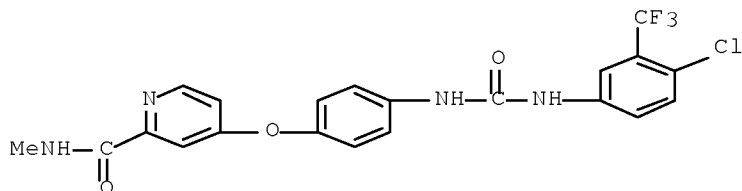
IT 284461-73-0, BAY 43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antitumor effect and potentiation or reduction in cytotoxic drug activity in human colon carcinoma cells by the Raf kinase inhibitor (RKI) BAY 43-9006 in relation to resistance to SN-38)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c(=O)amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-6 (Pharmacology)
 IT 51-21-8, 5-FU 33069-62-4, Paclitaxel 61825-94-3, Oxaliplatin
 86639-52-3, SN-38 284461-73-0, BAY 43-9006
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (antitumor effect and potentiation or reduction in cytotoxic drug activity
 in human colon carcinoma cells by the Raf kinase inhibitor (RKI) BAY
 43-9006 in relation to resistance to SN-38)
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 52 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:12705 HCAPLUS Full-text

DOCUMENT NUMBER: 140:349958

TITLE: Circadian rhythm in the regulation of the MAP kinase
 pathway - pitfall in the determination of surrogate
 parameters?

AUTHOR(S): Hilger, R. A.; Diaz-Carballo, D.; Bauer, S.; Kredtke,
 S.; Scheulen, M. E.; Seeber, S.; Strumberg, D.

CORPORATE SOURCE: Department of Internal Medicine (Cancer Research),
 West German Cancer Center, University of Essen Medical
 School, Essen, Germany

SOURCE: International Journal of Clinical Pharmacology and
 Therapeutics (2003), 41(12), 614-615
 CODEN: ICTHEK; ISSN: 0946-1965

PUBLISHER: Dustri-Verlag Dr. Karl Feistle

DOCUMENT TYPE: Journal

LANGUAGE: English

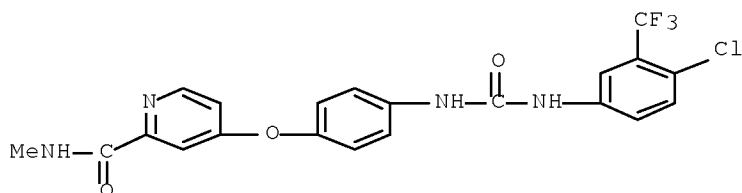
AB A method for the quantification of the inhibitory potency of BAY 43-9006, a
 novel potent and orally active inhibitor of Raf kinase, measuring the
 phosphorylated (activated) extracellular signal-regulated kinase (ERK) as a
 biomarker, was developed. A circadian rhythm in phosphorylation of ERK1/2
 proteins after phorbol myristate acetate stimulation was observed. It was
 demonstrated that biomarker measurements could be complicated by circadian
 variability of the specific mol. target. Phosphorylated ERK1/2 may serve as a
 biomarker for drugs targeting the mitogen-activated protein kinase cascade.
 However, the demonstrated circadian regulation demands strict protocols for
 the realization of biomarker analyses.

IT 284461-73-0, BAY 43-9006

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (circadian rhythm in regulation of MAP kinase pathway)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c
 arboxyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-1 (Pharmacology)

IT 284461-73-0, BAY 43-9006

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(circadian rhythm in regulation of MAP kinase pathway)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 53 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:476541 HCAPLUS Full-text

DOCUMENT NUMBER: 139:143192

TITLE: Activity of the Raf kinase inhibitor BAY 43-9006 in patients with advanced solid tumors

AUTHOR(S): DeGrendele, Heather

CORPORATE SOURCE: USA

SOURCE: Clinical Colorectal Cancer (2003), 3(1), 16-18

CODEN: CCCLCF; ISSN: 1533-0028

PUBLISHER: Cancer Information Group

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. BAY 43-9006 is the first orally active Raf kinase inhibitor to undergo clin. testing and has shown promise in the treatment of colorectal cancer. Treatment with BAY 43-9006 has resulted in stable disease in 37 % of patients across this phase I series, with 42 % of colorectal cancer patients achieving stable disease. Among patients achieving stable disease, 27 have been on therapy for over 6 mo without progression. Toxicity associated with this regimen is mild, with few grade 3/4 adverse events reported. Furthermore, fluorescence-activated cell sorter (FACS) anal. demonstrated that treatment with BAY 43-9006 could result in the inhibition of extracellular signal-regulated kinase (ERK) activation. Based on this phase I data, 2 phase II trials, including one in patients with colorectal cancer, have been initiated, and phase III trials are planned for 2003. At the 38th Annual Meeting of the American Society of Clin. Oncol., Vincent and colleagues reported on preclin. studies combining BAY 43-9006 with irinotecan, vinorelbine, or gemcitabine in human xenografts models. They demonstrated that BAY 43-9006 combined with cytotoxic or cytostatic agents is at least as efficacious as the individual agents administered alone. With this as rationale, multiple phase I/II studies are being designed to investigate the role of BAY 43-9006 in combination with standard chemotherapy.

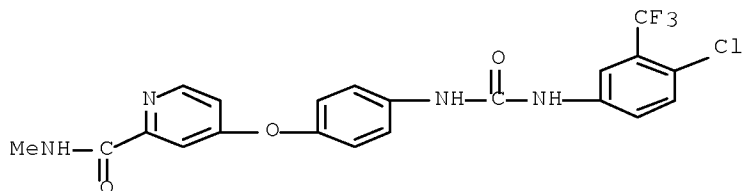
IT 284461-73-0, BAY 43-9006

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(activity of Raf kinase inhibitor BAY 43-9006 in patients with advanced solid tumors)

RN 284461-73-0 HCAPLUS

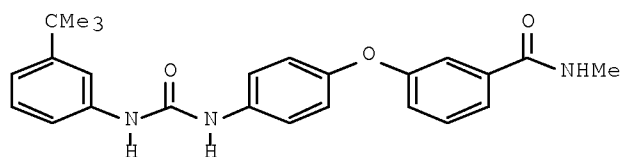
CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-0 (Pharmacology)
 IT 284461-73-0, BAY 43-9006
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (activity of Raf kinase inhibitor BAY 43-9006 in patients with advanced solid tumors)
 REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 54 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2002:615574 HCAPLUS Full-text
 DOCUMENT NUMBER: 137:169425
 TITLE: Preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors
 INVENTOR(S): Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Sibley, Robert N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.
 PATENT ASSIGNEE(S): Bayer Corporation, USA
 SOURCE: PCT Int. Appl., 125 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 5
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|-----------------|
| WO 2002062763 | A2 | 20020815 | WO 2002-US3361 | 20020207 <-- |
| WO 2002062763 | A3 | 20021010 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| US 20020165394 | A1 | 20021107 | US 2001-777920 | 20010207 <-- |
| AU 2002238042 | A1 | 20020819 | AU 2002-238042 | 20020207 <-- |
| AU 2004200722 | A1 | 20040318 | AU 2004-200722 | 20040224 <-- |
| AU 2004200722 | B2 | 20080110 | | |
| PRIORITY APPLN. INFO.: | | | US 2001-777920 | A 20010207 <-- |
| | | | US 1999-115877P | P 19990113 <-- |
| | | | US 1999-257266 | B2 19990225 <-- |
| | | | US 1999-425228 | B2 19991022 <-- |
| | | | AU 2000-25016 | A3 20000112 <-- |
| | | | US 2001-758548 | A2 20010112 <-- |
| | | | WO 2002-US3361 | W 20020207 <-- |
| OTHER SOURCE(S): | MARPAT 137:169425 | | | |
| GI | | | | |



II

AB Title compds., e.g., RNHCONHZOR1 [I; R = C₆H₄(CMe₃)-3, 2-methoxy-5-trifluoromethylphenyl, 4-chloro-3-trifluoromethylphenyl, 2-methoxy-3-quinolyl, etc.; R₁ = (un)substituted acylphenyl, -acylpyridinyl, etc.; Z = (un)substituted 1,3- or -1,4-phenylene] were prepared. Thus, 4-(H₂N)C₆H₄OC₆H₄(CONHMe)-4 (preparation given) was condensed with 3-(Me₃C)C₆H₄NH₂ and CO(OCCl₃)₂ to give title compound II. Data for biol. activity of title compds. were given.

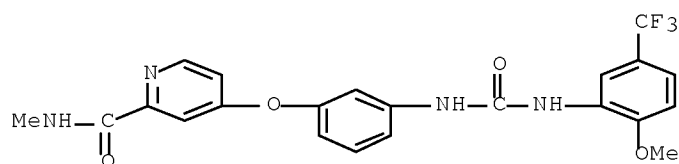
IT 284461-42-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors)

RN 284461-42-3 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D215-38

ICS C07D401-12; A61K031-4406; A61K031-47; A61P035-00; C07D401-12; C07D215-00; C07D213-00; C07D401-12; C07D215-00; C07D209-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT 228418-48-2P 284461-33-2P 284461-34-3P 284461-35-4P 284461-36-5P
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284461-51-4P 284461-52-5P 284461-53-6P 284461-54-7P
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284461-97-8P 284461-98-9P 284461-99-0P 284462-00-6P
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 447457-09-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase
 inhibitors)

L110 ANSWER 55 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:314913 HCAPLUS Full-text

DOCUMENT NUMBER: 136:340689

TITLE: Preparation of urea derivatives containing nitrogenous
 aromatic ring compounds as inhibitors of angiogenesis

INVENTOR(S): Funahashi, Yasuhiro; Tsuruoka, Akihiko; Matsukura,
 Masayuki; Haneda, Toru; Fukuda, Yoshio; Kamata,
 Junichi; Takahashi, Keiko; Matsushima, Tomohiro;
 Miyazaki, Kazuki; Nomoto, Kenichi; Watanabe, Tatsuo;
 Obaishi, Hiroshi; Yamaguchi, Atsumi; Suzuki, Sachi;
 Nakamura, Katsuji; Mimura, Fusayo; Yamamoto, Yuji;
 Matsui, Junji; Matsui, Kenji; Yoshiba, Takako; Suzuki,
 Yasuyuki; Arimoto, Itaru

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan

SOURCE: PCT Int. Appl., 699 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

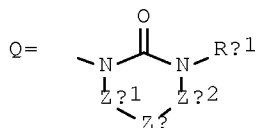
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|--------------|
| WO 2002032872 | A1 | 20020425 | WO 2001-JP9221 | 20011019 <-- |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | |
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| CA 2426461 | A1 | 20020425 | CA 2001-2426461 | 20011019 <-- |
| AU 2001095986 | A | 20020429 | AU 2001-95986 | 20011019 <-- |
| HU 2003002603 | A2 | 20031128 | HU 2003-2603 | 20011019 <-- |
| CN 1478078 | A | 20040225 | CN 2001-819710 | 20011019 <-- |
| EP 1415987 | A1 | 20040506 | EP 2001-976786 | 20011019 <-- |
| EP 1415987 | B1 | 20070228 | | |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR | | | |

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|---|-------------------|----------|------------------|-----------------|
| EP 1506962 | A2 | 20050216 | EP 2004-25700 | 20011019 <-- |
| EP 1506962 | A3 | 20050302 | | |
| EP 1506962 | B1 | 20080702 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR | | | | |
| NZ 525324 | A | 20050324 | NZ 2001-525324 | 20011019 <-- |
| JP 3712393 | B2 | 20051102 | JP 2002-536056 | 20011019 <-- |
| RU 2264389 | C2 | 20051120 | RU 2003-114740 | 20011019 <-- |
| AT 355275 | T | 20060315 | AT 2001-976786 | 20011019 <-- |
| AU 2001295986 | B2 | 20060817 | AU 2001-295986 | 20011019 <-- |
| EP 1777218 | A1 | 20070425 | EP 2006-23078 | 20011019 <-- |
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| CN 101024627 | A | 20070829 | CN 2007-10007096 | 20011019 <-- |
| CN 101029022 | A | 20070905 | CN 2007-10007097 | 20011019 <-- |
| ES 2282299 | T3 | 20071016 | ES 2001-976786 | 20011019 <-- |
| NO 2003001731 | A | 20030619 | NO 2003-1731 | 20030414 <-- |
| MX 2003PA03362 | A | 20030801 | MX 2003-PA3362 | 20030415 <-- |
| US 7253286 | B2 | 20070807 | US 2003-420466 | 20030418 <-- |
| US 20040053908 | A1 | 20040318 | | |
| ZA 2003003567 | A | 20040810 | ZA 2003-3567 | 20030508 <-- |
| JP 2005272474 | A | 20051006 | JP 2005-124034 | 20050421 <-- |
| US 20060247259 | A1 | 20061102 | US 2005-293785 | 20051202 <-- |
| US 20060160832 | A1 | 20060720 | US 2006-347749 | 20060203 <-- |
| AU 2006203099 | A1 | 20060810 | AU 2006-203099 | 20060719 <-- |
| AU 2006236039 | A1 | 20061207 | AU 2006-236039 | 20061116 <-- |
| AU 2006236039 | B2 | 20080522 | | |
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| PRIORITY APPLN. INFO.: | | | JP 2000-320420 | A 20001020 <-- |
| | | | JP 2000-386195 | A 20001220 <-- |
| | | | JP 2001-46685 | A 20010222 <-- |
| | | | AU 2001-295986 | A3 20011019 <-- |
| | | | AU 2001-95986 | TO 20011019 <-- |
| | | | CN 2001-819710 | A3 20011019 <-- |
| | | | EP 2001-976786 | A3 20011019 <-- |
| | | | JP 2002-536056 | A3 20011019 <-- |
| | | | WO 2001-JP9221 | W 20011019 <-- |
| | | | US 2003-420466 | A3 20030418 <-- |
| | | | US 2005-293785 | A1 20051202 |
| OTHER SOURCE(S): | MARPAT 136:340689 | | | |
| GI | | | | |



AB N-aryl or N-heteroarylurea derivs. represented by the general formula Ag-Xg-Yg-Tg1 or salts thereof, or hydrates of both [wherein Ag = (un)substituted C6-14 aryl or 5- to 14-membered heterocyclic group; Xg = single bond, O, S, C1-6 alkylene, SO, SO2, (un)substituted NH; Yg = (un)substituted C6-14 aryl, 5- to 14-membered heterocyclic group, C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14

aryl-C1-6 alkyl, 5- to 14-membered heteroaryl-C1-6 alkyl, (CH₂)_gSO₂ (g = 1-8), (CH₂)_{fa}CH:CH(CH₂)_{fb} (fa, fb = 0, 1,2,3), etc.; and Tg1 = a group of the general formula -Eg-CO-NRg1(Zg) or Q; wherein Eg = a single bond, (un)substituted NH; Rg1 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 aliphatic hydrocarbyl, etc.; Zg = C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl, etc.; Zg1, Zg2 = (a) a single bond, (b) C1-6 alkylene optionally having ≥1 atoms selected from O, S, and N in the middle or the terminus of the chain and optionally substituted with oxo, (c) (un)substituted C2-6 alkenyl] are prepared These compds. are also inhibitors of vascular endothelial growth factor receptor kinase (VEGFR2 kinase) and are useful as antitumor agents against hemangioma, pancreatic cancer, stomach cancer, colon cancer, breast cancer, prostate cancer, lung cancer, brain tumor, leukemia, or ovarian cancer, as cancer metastasis inhibitors, and for the treatment of retina neovascularization, diabetic retinopathy, atherosclerosis, or inflammatory diseases such as osteoarthritis, rheumatoid arthritis, psoriasis, or delayed hypersensitivity. Thus, to solution of 334 mg 4-[6-(4-benzoyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenylamine in 4 mL DMF were added 0.066 mL pyridine and 0.102 mL Ph chlorocarbonate and stirred at room temperature for 2.5 h to give 330 mg N-[4-[6-(4-benzoyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea which (260 mg) was hydrogenolyzed over platinum oxide in ethanol overnight to give 160 mg N-[4-[6-(4-hydroxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea (I). I showed IC₅₀ of 0.02 nM for inhibiting the vascular endothelial growth factor (VEGF)-stimulated sandwich tube formation in vascular endothelial cell.

IT 417714-74-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

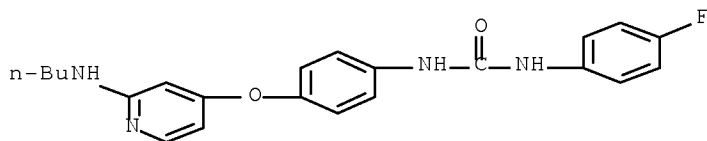
(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

RN 417714-74-0 HCAPLUS

CN Urea, N-[4-[[2-(butylamino)-4-pyridinyl]oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



IC ICM C07D213-74

ICS C07D213-75; C07D215-48; C07D239-47; C07D401-12; C07D401-14; C07D413-12; C07D405-12; C07D409-12; C07D413-12; C07D417-12; C07D417-14; C07D471-14; C07D491-048; C07D495-04; A61K031-4709; A61K031-47; A61K031-5377; A61K031-496; A61K031-4545

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 27

| | | | | | |
|----|--------------|--------------|--------------|--------------|--------------|
| IT | 398487-65-5P | 417712-82-4P | 417712-83-5P | 417712-84-6P | 417712-85-7P |
| | 417712-86-8P | 417712-87-9P | 417712-88-0P | 417712-89-1P | 417712-90-4P |
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| | 417713-01-0P | 417713-02-1P | 417713-03-2P | 417713-04-3P | 417713-05-4P |

| | | | | |
|--------------|--------------|--------------|--------------|--------------|
| 417713-06-5P | 417713-08-7P | 417713-11-2P | 417713-12-3P | 417713-13-4P |
| 417713-14-5P | 417713-15-6P | 417713-16-7P | 417713-17-8P | 417713-18-9P |
| 417713-19-0P | 417713-20-3P | 417713-21-4P | 417713-23-6P | 417713-25-8P |
| 417713-26-9P | 417713-27-0P | 417713-28-1P | 417713-29-2P | 417713-30-5P |
| 417713-31-6P | 417713-32-7P | 417713-33-8P | 417713-34-9P | 417713-35-0P |
| 417713-36-1P | 417713-37-2P | 417713-38-3P | 417713-39-4P | 417713-40-7P |
| 417713-42-9P | 417713-44-1P | 417713-45-2P | 417713-47-4P | 417713-49-6P |
| 417713-51-0P | 417713-57-6P | 417713-59-8P | 417713-60-1P | 417713-62-3P |
| 417713-63-4P | 417713-64-5P | 417713-65-6P | 417713-66-7P | 417713-67-8P |
| 417713-68-9P | 417713-69-0P | 417713-70-3P | 417713-71-4P | 417713-75-8P |
| 417713-76-9P | 417713-77-0P | 417713-84-9P | 417713-85-0P | 417713-87-2P |
| 417713-90-7P | 417713-93-0P | 417713-94-1P | 417713-95-2P | 417713-96-3P |
| 417713-97-4P | 417713-98-5P | 417713-99-6P | 417714-00-2P | 417714-01-3P |
| 417714-02-4P | 417714-03-5P | 417714-05-7P | 417714-06-8P | 417714-07-9P |
| 417714-08-0P | 417714-09-1P | 417714-11-5P | 417714-12-6P | 417714-14-8P |
| 417714-15-9P | 417714-16-0P | 417714-17-1P | 417714-18-2P | 417714-19-3P |
| 417714-20-6P | 417714-21-7P | 417714-22-8P | 417714-23-9P | 417714-24-0P |
| 417714-25-1P | 417714-26-2P | 417714-27-3P | 417714-28-4P | 417714-29-5P |
| 417714-30-8P | 417714-31-9P | 417714-32-0P | 417714-33-1P | 417714-36-4P |
| 417714-37-5P | 417714-38-6P | 417714-39-7P | 417714-40-0P | 417714-41-1P |
| 417714-42-2P | 417714-43-3P | 417714-44-4P | 417714-45-5P | 417714-46-6P |
| 417714-47-7P | 417714-48-8P | 417714-49-9P | 417714-50-2P | 417714-51-3P |
| 417714-52-4P | 417714-53-5P | 417714-54-6P | 417714-55-7P | 417714-58-0P |
| 417714-59-1P | 417714-60-4P | 417714-62-6P | 417714-63-7P | 417714-64-8P |
| 417714-65-9P | 417714-66-0P | 417714-67-1P | 417714-68-2P | 417714-69-3P |
| 417714-70-6P | 417714-71-7P | 417714-72-8P | 417714-73-9P | |
| 417714-74-0P | 417714-75-1P | 417714-76-2P | 417714-77-3P | |
| 417714-78-4P | 417714-79-5P | 417714-80-8P | 417714-81-9P | |
| 417714-82-0P | 417714-83-1P | 417714-84-2P | 417714-85-3P | 417714-86-4P |
| 417714-87-5P | 417714-89-7P | 417714-90-0P | 417714-91-1P | 417714-92-2P |
| 417714-93-3P | 417714-94-4P | 417714-95-5P | 417714-96-6P | |
| 417714-97-7P | 417714-98-8P | 417714-99-9P | 417715-00-5P | |
| 417715-01-6P | 417715-02-7P | 417715-03-8P | 417715-05-0P | 417715-07-2P |
| 417715-08-3P | 417715-09-4P | 417715-10-7P | 417715-11-8P | 417715-12-9P |
| 417715-13-0P | 417715-14-1P | 417715-15-2P | 417715-16-3P | 417715-17-4P |
| 417715-18-5P | 417715-19-6P | 417715-20-9P | 417715-21-0P | 417715-22-1P |
| 417715-23-2P | 417715-24-3P | 417715-25-4P | 417715-27-6P | 417715-28-7P |
| 417715-29-8P | 417715-30-1P | 417715-31-2P | 417715-32-3P | 417715-33-4P |
| 417715-34-5P | 417715-35-6P | 417715-36-7P | 417715-37-8P | 417715-39-0P |
| 417715-40-3P | 417715-42-5P | 417715-44-7P | 417715-46-9P | 417715-47-0P |
| 417715-49-2P | 417715-51-6P | 417715-53-8P | 417715-55-0P | 417715-57-2P |
| 417715-59-4P | 417715-61-8P | 417715-63-0P | 417715-65-2P | 417715-66-3P |
| 417715-67-4P | 417715-68-5P | 417715-69-6P | 417715-70-9P | |

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

| | | | | | |
|----|--------------|--------------|--------------|--------------|--------------|
| IT | 417715-71-0P | 417715-72-1P | 417715-73-2P | 417715-74-3P | 417715-75-4P |
| | 417715-76-5P | 417715-77-6P | 417715-78-7P | 417715-79-8P | 417715-81-2P |
| | 417715-83-4P | 417715-85-6P | 417715-86-7P | 417715-88-9P | 417715-90-3P |
| | 417715-91-4P | 417715-93-6P | 417715-95-8P | 417715-97-0P | 417715-99-2P |
| | 417716-01-9P | 417716-03-1P | 417716-05-3P | 417716-06-4P | 417716-07-5P |
| | 417716-08-6P | 417716-09-7P | 417716-10-0P | 417716-12-2P | 417716-13-3P |
| | 417716-14-4P | 417716-15-5P | 417716-16-6P | 417716-17-7P | 417716-18-8P |
| | 417716-19-9P | 417716-20-2P | 417716-21-3P | 417716-22-4P | 417716-23-5P |
| | 417716-24-6P | 417716-25-7P | 417716-26-8P | 417716-27-9P | 417716-28-0P |
| | 417716-29-1P | 417716-30-4P | 417716-31-5P | 417716-32-6P | 417716-33-7P |
| | 417716-34-8P | 417716-35-9P | 417716-36-0P | 417716-37-1P | 417716-38-2P |

| | | | | |
|--------------|--------------|--------------|--------------|--------------|
| 417716-39-3P | 417716-40-6P | 417716-41-7P | 417716-43-9P | 417716-44-0P |
| 417716-45-1P | 417716-46-2P | 417716-47-3P | 417716-48-4P | 417716-49-5P |
| 417716-50-8P | 417716-51-9P | 417716-52-0P | 417716-53-1P | 417716-54-2P |
| 417716-55-3P | 417716-56-4P | 417716-57-5P | 417716-58-6P | 417716-59-7P |
| 417716-60-0P | 417716-61-1P | 417716-62-2P | 417716-63-3P | 417716-64-4P |
| 417716-65-5P | 417716-66-6P | 417716-67-7P | 417716-68-8P | 417716-69-9P |
| 417716-70-2P | 417716-71-3P | 417716-72-4P | 417716-73-5P | 417716-74-6P |
| 417716-75-7P | 417716-76-8P | 417716-77-9P | 417716-78-0P | 417716-79-1P |
| 417716-80-4P | 417716-81-5P | 417716-82-6P | 417716-83-7P | 417716-84-8P |
| 417716-85-9P | 417716-86-0P | 417716-87-1P | 417716-88-2P | 417716-89-3P |
| 417716-90-6P | 417716-91-7P | 417716-92-8P | 417716-93-9P | 417716-94-0P |
| 417716-95-1P | 417716-96-2P | 417716-97-3P | 417716-98-4P | 417716-99-5P |
| 417717-00-1P | 417717-01-2P | 417717-02-3P | 417717-03-4P | 417717-04-5P |
| 417717-05-6P | 417717-06-7P | 417717-07-8P | 417717-08-9P | 417717-09-0P |
| 417717-10-3P | 417717-11-4P | 417717-14-7P | 417717-15-8P | 417717-16-9P |
| 417717-17-0P | 417717-18-1P | 417717-19-2P | 417717-20-5P | 417717-22-7P |
| 417717-23-8P | 417717-24-9P | 417717-25-0P | 417717-26-1P | 417717-27-2P |
| 417717-28-3P | 417717-29-4P | 417717-30-7P | 417717-31-8P | 417717-32-9P |
| 417717-33-0P | 417717-34-1P | 417717-35-2P | 417717-36-3P | 417717-37-4P |
| 417717-38-5P | 417717-40-9P | 417717-41-0P | 417717-43-2P | 417717-44-3P |
| 417717-46-5P | 417717-47-6P | 417717-48-7P | 417717-49-8P | 417717-51-2P |
| 417717-52-3P | 417717-53-4P | 417717-55-6P | 417717-57-8P | 417717-58-9P |
| 417717-60-3P | 417717-62-5P | 417717-63-6P | 417717-64-7P | 417717-66-9P |
| 417717-67-0P | 417717-68-1P | 417717-69-2P | 417717-70-5P | 417717-71-6P |
| 417717-72-7P | 417717-73-8P | 417717-74-9P | 417717-75-0P | 417717-76-1P |
| 417717-77-2P | 417717-78-3P | 417717-79-4P | 417717-81-8P | 417717-83-0P |
| 417717-86-3P | 417717-87-4P | 417717-88-5P | 417717-89-6P | 417717-93-2P |
| 417717-95-4P | 417717-97-6P | 417717-99-8P | 417718-00-4P | 417718-02-6P |
| 417718-04-8P | 417718-06-0P | 417718-10-6P | 417718-11-7P | |
| 417718-13-9P | 417718-15-1P | 417718-17-3P | | |
| 417718-19-5P | 417718-21-9P | 417718-23-1P | 417718-25-3P | |
| 417718-26-4P | 417718-28-6P | 417718-30-0P | 417718-31-1P | 417718-32-2P |
| 417718-34-4P | 417718-35-5P | 417718-36-6P | 417718-37-7P | 417718-39-9P |
| 417718-40-2P | 417718-41-3P | 417718-42-4P | 417718-43-5P | 417718-44-6P |
| 417718-45-7P | 417718-46-8P | 417718-47-9P | 417718-48-0P | 417718-49-1P |
| 417718-50-4P | 417718-51-5P | 417718-52-6P | 417718-53-7P | 417718-54-8P |
| 417718-55-9P | 417718-56-0P | 417718-57-1P | | |

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

| | | | | | |
|----|--------------------------|-------------------------------|--------------|--------------|--------------|
| IT | 399-95-1P | 3898-47-3P | 4792-60-3P | 5264-02-8P | 6980-08-1P |
| | 7251-09-4P, | 4-Amino-2-methoxybenzonitrile | 14549-38-3P | 17424-90-7P | |
| | 17576-39-5P | 17614-10-7P | 18031-97-5P | 39142-40-0P, | Phenyl |
| | N-(2-thiazolyl)carbamate | 65141-00-6P | 65141-04-0P | 74889-21-7P | |
| | 81479-55-2P | 96783-89-0P | 97480-55-2P | 105130-28-7P | 124041-03-8P |
| | 130035-46-0P | 185220-68-2P | 190060-72-1P | 221040-07-9P | 286371-87-7P |
| | 347151-53-5P | 417720-95-7P | 417720-96-8P | 417720-97-9P | 417720-98-0P |
| | 417720-99-1P | 417721-00-7P | 417721-01-8P | 417721-02-9P | 417721-03-0P |
| | 417721-04-1P | 417721-05-2P | 417721-06-3P | 417721-07-4P | 417721-08-5P |
| | 417721-09-6P | 417721-10-9P | 417721-11-0P | 417721-12-1P | 417721-13-2P |
| | 417721-14-3P | 417721-15-4P | 417721-16-5P | 417721-17-6P | 417721-18-7P |
| | 417721-19-8P | 417721-20-1P | 417721-21-2P | 417721-22-3P | 417721-23-4P |
| | 417721-24-5P | 417721-25-6P | 417721-26-7P | 417721-27-8P | 417721-28-9P |
| | 417721-29-0P | 417721-30-3P | 417721-31-4P | 417721-32-5P | 417721-33-6P |
| | 417721-34-7P | 417721-35-8P | 417721-36-9P | 417721-37-0P | 417721-38-1P |
| | 417721-39-2P | 417721-40-5P | 417721-41-6P | 417721-42-7P | 417721-43-8P |
| | 417721-44-9P | 417721-45-0P | 417721-46-1P | 417721-47-2P | 417721-48-3P |

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| | | | | |
|-------------------------|--------------|-------------------------|-------------------------|--------------|
| 417721-49-4P | 417721-50-7P | 417721-51-8P | 417721-52-9P | 417721-53-0P |
| 417721-54-1P | 417721-55-2P | 417721-56-3P | 417721-57-4P | 417721-58-5P |
| 417721-59-6P | 417721-60-9P | 417721-61-0P | 417721-62-1P | 417721-63-2P |
| 417721-64-3P | 417721-65-4P | 417721-66-5P | 417721-67-6P | 417721-68-7P |
| 417721-69-8P | 417721-70-1P | 417721-71-2P | 417721-72-3P | 417721-73-4P |
| 417721-74-5P | 417721-75-6P | 417721-76-7P | 417721-77-8P | |
| 417721-78-9P | 417721-79-0P | 417721-80-3P | 417721-81-4P | |
| 417721-82-5P | 417721-83-6P | 417721-84-7P | 417721-85-8P | |
| 417721-86-9P | 417721-87-0P | 417721-88-1P | 417721-89-2P | 417721-90-5P |
| 417721-91-6P | 417721-92-7P | 417721-93-8P | 417721-94-9P | |
| 417721-95-0P | 417721-96-1P | 417721-97-2P | 417721-98-3P | 417721-99-4P |
| 417722-00-0P | 417722-01-1P | 417722-02-2P | 417722-03-3P | |
| 417722-04-4P | 417722-05-5P | 417722-06-6P | 417722-07-7P | 417722-08-8P |
| 417722-10-2P | 417722-11-3P | 417722-12-4P | 417722-13-5P | 417722-14-6P |
| 417722-15-7P | 417722-16-8P | 417722-17-9P | 417722-18-0P | 417722-19-1P |
| 417722-20-4P | 417722-21-5P | 417722-22-6P | 417722-23-7P | 417722-24-8P |
| 417722-25-9P | 417722-26-0P | 417722-27-1P | 417722-28-2P | 417722-29-3P |
| 417722-30-6P | 417722-31-7P | 417722-32-8P | 417722-33-9P | 417722-34-0P |
| 417722-35-1P | 417722-36-2P | 417722-37-3P | 417722-38-4P | 417722-39-5P |
| 417722-40-8P | 417722-41-9P | 417722-42-0P | 417722-43-1P | 417722-44-2P |
| 417722-45-3P | 417722-46-4P | 417722-47-5P | 417722-48-6P | 417722-49-7P |
| 417722-50-0P | 417722-51-1P | 417722-52-2P | 417722-53-3P | 417722-54-4P |
| 417722-55-5P | 417722-56-6P | 417722-57-7P | 417722-58-8P | 417722-59-9P |
| 417722-60-2P | 417722-61-3P | 417722-62-4P | 417722-63-5P | 417722-64-6P |
| 417722-65-7P | 417722-66-8P | 417722-67-9P | 417722-69-1P | 417722-71-5P |
| 417722-73-7P | 417722-75-9P | 417722-76-0P | 417722-77-1P | 417722-78-2P |
| 417722-79-3P | 417722-81-7P | 417722-82-8P | 417722-83-9P | 417722-85-1P |
| 417722-87-3P | 417722-89-5P | 417722-91-9P | 417722-93-1P | 417722-95-3P |
| 417722-97-5P | 417722-99-7P | 417723-01-4P | 417723-03-6P | 417723-05-8P |
| 417723-07-0P | 417723-09-2P | 417723-11-6P | 417723-13-8P | 417723-15-0P |
| 417723-17-2P | 417723-19-4P | 417723-21-8P | 417723-23-0P | 417723-25-2P |
| 417723-27-4P | 417723-29-6P | 417723-31-0P | 417723-33-2P | 417723-35-4P |
| 417723-37-6P | | | | |

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

| | | | | | |
|----|--------------|-------------------------|--------------|--------------|--------------|
| IT | 417723-39-8P | 417723-41-2P | 417723-43-4P | 417723-44-5P | 417723-45-6P |
| | 417723-49-0P | 417723-51-4P | 417723-53-6P | 417723-54-7P | |
| | 417723-55-8P | 417723-56-9P | 417723-57-0P | 417723-58-1P | 417723-59-2P |
| | 417723-60-5P | 417723-61-6P | 417723-62-7P | 417723-63-8P | 417723-64-9P |
| | 417723-65-0P | 417723-66-1P | 417723-67-2P | 417723-68-3P | 417723-70-7P |
| | 417723-71-8P | 417723-72-9P | 417723-73-0P | 417723-74-1P | 417723-75-2P |
| | 417723-76-3P | 417723-77-4P | 417723-78-5P | 417723-80-9P | 417723-81-0P |
| | 417723-82-1P | 417723-83-2P | 417723-84-3P | 417723-85-4P | 417723-87-6P |
| | 417723-89-8P | 417723-91-2P | 417723-93-4P | 417723-94-5P | 417723-95-6P |
| | 417723-96-7P | 417723-97-8P | 417723-98-9P | 417723-99-0P | 417724-00-6P |
| | 417724-01-7P | 417724-02-8P | 417724-03-9P | 417724-04-0P | 417724-05-1P |
| | 417724-06-2P | 417724-07-3P | 417724-08-4P | 417724-09-5P | 417724-10-8P |
| | 417724-11-9P | 417724-12-0P | 417724-13-1P | 417724-14-2P | 417724-15-3P |
| | 417724-16-4P | 417724-17-5P | 417724-18-6P | 417724-19-7P | 417724-20-0P |
| | 417724-21-1P | 417724-24-4P | 417724-25-5P | 417724-26-6P | 417724-27-7P |
| | 417724-28-8P | 417724-29-9P | 417724-30-2P | 417724-31-3P | 417724-32-4P |
| | 417724-33-5P | 417724-34-6P | 417724-35-7P | 417724-36-8P | 417724-37-9P |
| | 417724-38-0P | 417724-39-1P | 417724-40-4P | 417724-41-5P | 417724-42-6P |
| | 417724-43-7P | 417724-44-8P | 417724-45-9P | 417724-46-0P | 417724-47-1P |
| | 417724-48-2P | 417724-49-3P | 417724-50-6P | 417724-51-7P | 417724-52-8P |
| | 417724-53-9P | 417724-54-0P | 417724-55-1P | 417724-56-2P | 417724-57-3P |
| | 417724-58-4P | 417724-59-5P | 417724-60-8P | 417724-61-9P | 417724-62-0P |

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417724-63-1P 417724-64-2P 417724-65-3P 417724-66-4P 417724-67-5P
417724-68-6P 417724-69-7P 417724-70-0P 417724-71-1P 417724-72-2P
417724-74-4P, 4-(4-Aminophenoxy)pyrimidine 417724-75-5P,
N-(4-(7-Benzyloxy-6-cyano-4-quinolyloxy)phenyl)-N'-(4-fluorophenyl)urea
417724-80-2P, N-(3-(6,7-Dimethoxy-4-quinolinyloxy)propyl)phthalimide
417724-81-3P 417724-86-8P, N-Cyclopropyl-5-[(2-(2-chloroacetyl-amino)-4-
pyridyl)oxy]-1H-1-indolecarboxamide 417724-87-9P, N-Cyclopropyl-5-[(2-
((3-bromopropionyl)amino)-4-pyridyl)oxy]-1H-1-indolecarboxamide
417724-88-0P, 4-[2-[(4-[3-Chloro-4-[(phenoxy-carbonyl)amino]phenoxy]-2-
pyridyl)amino]-2-oxoethyl]-1-piperidinecarboxylic acid tert-butyl ester
417724-89-1P, N-Phenyl-3-chloro-5-[(2-[(4-piperidyl)carbonyl]amino)-4-
pyridyl)oxy]-1H-1-indolecarboxamide 417724-90-4P, 2-[(4-
Chlorobutyl)amino]-4-(4-nitrophenoxy)pyridine 417724-91-5P
417724-92-6P, 4-(2-Chloro-6-[(diphenylmethylene)amino]pyridin-3-yloxy)-6,7-
dimethoxyquinoline 417724-94-8P, (4-(4-Nitrophenoxy)-7-methoxyquinolin-6-
yl)carbamic acid benzyl ester 417724-95-9P,
7-(((2R)-2-(Triethylsilyloxy)-3-(pyrrolidin-1-yl)propyl)oxy)-4-(1H-indol-5-
yloxy)quinoline-6-carbonitrile 417724-96-0P, N-(2-Fluoroethyl)-5-(6-
cyano-7-[(2-(1-(tert-butoxycarbonyl)piperidin-4-yl)ethyl)oxy]quinolin-4-
yloxy)indole-1-carboxamide 417724-98-2P, 4-(3-Chloro-4-
(((cyclopropylamino)carbonyl)amino)phenoxy)-7-((4-piperidyl)methoxy)-6-
quinolinecarboxamide 417724-99-3P, N-(4-(6-Cyano-7-hydroxy-4-
quinolinyloxy)-2-chlorophenyl)-N'-cyclopropylurea 417725-00-9P,
4-(4-Amino-3-chlorophenoxy)-6-cyano-7-hydroxyquinoline 417725-01-0P,
2-Amino-4-(4-aminophenoxy)-3-aminopyridine 417725-02-1P,
4-(4-Nitrophenoxy)-6-(4-(pyrrolidin-1-yl)phenyl)-7H-pyrrolo[2,3-
d]pyrimidine 417725-05-4P, N'-(4-Benzyloxy-2-methylphenyl)-N-(4-
fluorophenyl)urea 417725-08-7P, 6-Cyano-4-(3-fluoro-4-nitrophenoxy)-7-
hydroxyquinoline 417725-09-8P, 2-Amino-4-(4-nitrophenoxy)-3-
nitropyridine

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 56 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:850357 HCAPLUS Full-text

DOCUMENT NUMBER: 137:352907

TITLE: Preparation of quinolyl, isoquinolyl or pyridyl-ureas
as inhibitors of raf kinase for the treatment of
tumors and/or cancerous cell growth

INVENTOR(S): Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill
E.; Robert, Sibley N.; Monahan, Mary-Katherine;
Renick, Joel; Gunn, David E.; Lowinger, Timothy B.;
Scott, William J.; Smith, Roger A.

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 63 pp., Cont.-in-part of U.S.
Ser. No. 758,548.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

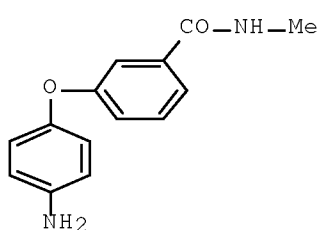
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------|------|----------|-----------------|--------------|
| US 20020165394 | A1 | 20021107 | US 2001-777920 | 20010207 <-- |

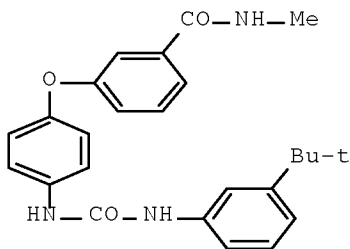
10/590724

| | | | | |
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| CA 2549558 | A1 | 20000720 | CA 2000-2549558 | 20000112 <-- |
| CN 1721397 | A | 20060118 | CN 2005-10089504 | 20000112 <-- |
| EP 1690853 | A1 | 20060816 | EP 2005-28442 | 20000112 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| ZA 2001005751 | A | 20030714 | ZA 2001-5751 | 20010712 <-- |
| US 20020137774 | A1 | 20020926 | US 2001-907970 | 20010719 <-- |
| WO 2002062763 | A2 | 20020815 | WO 2002-US3361 | 20020207 <-- |
| WO 2002062763 | A3 | 20021010 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002238042 | A1 | 20020819 | AU 2002-238042 | 20020207 <-- |
| US 20030139605 | A1 | 20030724 | US 2002-71248 | 20020211 <-- |
| AU 2004200722 | A1 | 20040318 | AU 2004-200722 | 20040224 <-- |
| AU 2004200722 | B2 | 20080110 | | |
| JP 2006328075 | A | 20061207 | JP 2006-190034 | 20060711 <-- |
| US 20080032979 | A1 | 20080207 | US 2007-845595 | 20070827 <-- |
| PRIORITY APPLN. INFO.: | | | US 1999-115877P | P 19990113 <-- |
| | | | US 1999-257266 | B2 19990225 <-- |
| | | | US 1999-425228 | B2 19991022 <-- |
| | | | US 2001-758548 | A2 20010112 <-- |
| | | | US 1999-115878P | P 19990113 <-- |
| | | | AU 2000-25016 | A3 20000112 <-- |
| | | | CA 2000-2359510 | A3 20000112 <-- |
| | | | CN 2000-802685 | A3 20000112 <-- |
| | | | EP 2000-903239 | A3 20000112 <-- |
| | | | JP 2000-593580 | A3 20000112 <-- |
| | | | US 2001-777920 | A 20010207 <-- |
| | | | US 2001-948915 | A1 20010910 <-- |
| | | | WO 2002-US3361 | W 20020207 <-- |

OTHER SOURCE(S): MARPAT 137:352907
GI



II



III

AB Title compds. B-NHCONH-L-(M-L1)q (I) [B = (un)substituted pyridyl, quinolinyl, isoquinolinyl; L = 5 or 6 membered cyclic structure; L1 = substituted cyclic moiety having at least 5 members; M = bridging group having at least one atom; q = 1-3; with proviso that L and L1 contain 0-4 hetero atoms, e.g., N, O and

S] and their pharmaceutically acceptable salts were prepared. For example, coupling of aniline II, e.g., prepared from Et 3-hydroxybenzoate in 4-steps, with bis(trichloromethyl)carbonate followed by 3-tert-butyraniline afforded urea III. In in vitro raf kinase assays, 112-specific examples of compds. I inhibited kinase activity with IC50 values ranging from 10 nM-10 µM. Compds. I are useful for the treatment of cancerous cell growth mediated by raf kinase.

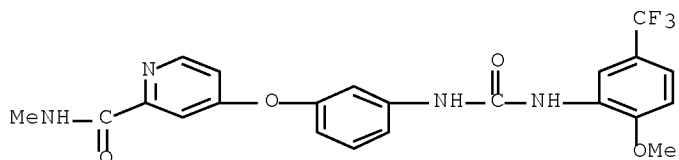
IT 284461-42-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of quinolyl, isoquinolyl or pyridyl-ureas as inhibitors of raf kinase)

RN 284461-42-3 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D217-22

ICS C07D215-38

INCL 546143000

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT 228418-48-2P 284461-33-2P 284461-34-3P 284461-35-4P 284461-36-5P
 284461-37-6P 284461-38-7P 284461-39-8P 284461-40-1P 284461-41-2P
 284461-42-3P 284461-43-4P 284461-44-5P
 284461-45-6P 284461-46-7P 284461-47-8P
 284461-48-9P 284461-49-0P 284461-50-3P
 284461-51-4P 284461-52-5P 284461-53-6P 284461-54-7P
 284461-55-8P 284461-56-9P 284461-57-0P 284461-58-1P
 284461-59-2P 284461-60-5P 284461-61-6P 284461-62-7P
 284461-63-8P 284461-64-9P 284461-65-0P 284461-66-1P 284461-67-2P
 284461-68-3P 284461-69-4P 284461-70-7P 284461-71-8P 284461-72-9P
 284461-73-0P 284461-74-1P 284461-75-2P
 284461-76-3P 284461-77-4P 284461-78-5P 284461-79-6P
 284461-80-9P 284461-81-0P 284461-82-1P
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 284461-94-5P 284461-95-6P 284461-96-7P 284461-97-8P
 284461-98-9P 284462-00-6P 284462-01-7P 284462-02-8P
 284462-03-9P 284462-04-0P 284462-05-1P 284462-07-3P 284462-08-4P
 284462-09-5P 284462-10-8P 284462-11-9P 284462-12-0P 284462-13-1P
 284462-15-3P 284462-16-4P 284462-17-5P 284462-18-6P
 284462-19-7P 284462-20-0P 284462-21-1P
 284462-22-2P 284462-23-3P 284462-24-4P
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 284462-29-9P 284462-30-2P 284462-31-3P
 284462-32-4P 284462-34-6P 284462-35-7P 284462-70-0P
 284670-98-0P 432050-20-9P, N-(4-tert-Butylpyridyl)-N'-(4-(4-

chlorophenoxy)phenyl) Urea 432050-22-1P 432050-23-2P 432050-24-3P
 432050-25-4P 432050-26-5P 432050-27-6P 432050-28-7P 432050-52-7P
 447457-08-1P 447457-09-2P 474642-44-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(drug candidate; preparation of quinolyl, isoquinolyl or pyridyl-ureas as
 inhibitors of raf kinase)

L110 ANSWER 57 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:732413 HCAPLUS Full-text

DOCUMENT NUMBER: 138:362126

TITLE: Benzodiazepine inhibitors of the MMPs and TACE

AUTHOR(S): Nelson, Frances C.; Delos Santos, Efren; Levin, Jeremy
 I.; Chen, James M.; Skotnicki, Jerauld S.; DiJoseph,
 John F.; Sharr, Michele A.; Sung, Amy; Killar, Loran
 M.; Cowling, Rebecca; Jin, Guixian; Roth, Catherine
 E.; Albright, J. Donald

CORPORATE SOURCE: Wyeth Research, Pearl River, NY, 10965, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2002
), 12(20), 2867-2870

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 138:362126

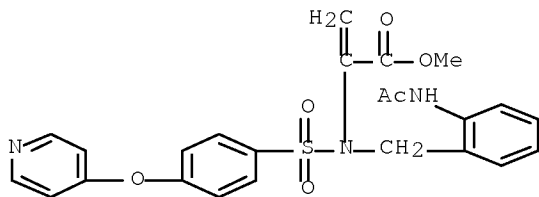
AB A series of benzodiazepine inhibitors of the MMPs and TACE has been developed.
 These compds. display an interesting selectivity profile and should be useful
 tools for exploring the biol. relevance of such selectivity.

IT 522623-58-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (benzodiazepine inhibitors of MMPs and TACE)

RN 522623-58-1 HCAPLUS

CN 2-Propenoic acid, 2-[[[2-(acetylamino)phenyl)methyl][[4-(4-
 pyridinyloxy)phenyl]sulfonyl]amino]-, methyl ester (CA INDEX NAME)



CC 1-3 (Pharmacology)

| | | | | | |
|----|--------------|--------------|--------------|--------------|--------------|
| IT | 85622-74-8P | 232950-28-6P | 233754-49-9P | 233754-50-2P | 233754-53-5P |
| | 233754-54-6P | 233754-61-5P | 233754-64-8P | 233754-67-1P | 233754-68-2P |
| | 233754-69-3P | 233754-71-7P | 233754-73-9P | 233754-75-1P | 233754-80-8P |
| | 233754-83-1P | 233754-86-4P | 233754-87-5P | 233754-88-6P | 233754-90-0P |
| | 233754-91-1P | 233754-93-3P | 233754-96-6P | 233754-99-9P | 233755-06-1P |
| | 233755-35-6P | 233755-36-7P | 233755-41-4P | 233755-56-1P | 233755-57-2P |
| | 233755-59-4P | 233755-60-7P | 233755-61-8P | 233755-62-9P | 233755-63-0P |
| | 233755-71-0P | 233755-72-1P | 233755-73-2P | 233755-75-4P | 287121-33-9P |
| | 522623-54-7P | 522623-55-8P | 522623-56-9P | 522623-57-0P | |

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522623-58-1P 522623-59-2P 522623-60-5P
522623-61-6P 522623-62-7P 522623-63-8P 522623-64-9P
522623-65-0P 522623-66-1P 522623-67-2P 522623-68-3P 522623-83-2P
522623-87-6P 597564-87-9P 612491-93-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(benzodiazepine inhibitors of MMPs and TACE)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 58 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:785445 HCAPLUS Full-text

DOCUMENT NUMBER: 138:296904

TITLE: BAY 43-9006: Preclinical data

AUTHOR(S): Wilhelm, Scott; Chien, Du-Shieng

CORPORATE SOURCE: Bayer Research Center, Institute for Preclinical Drug
Development, Pharmaceutical Division, Bayer
Corporation, West Haven, CT, 06516, USA

SOURCE: Current Pharmaceutical Design (2002), 8(25),
2255-2257

CODEN: CPDEFP; ISSN: 1381-6128

PUBLISHER: Bentham Science Publishers

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

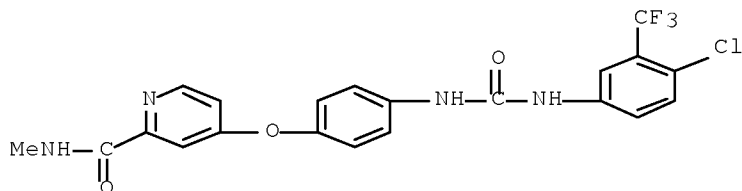
AB A review. The drug design and discovery efforts described in the previous
section led to the development of a novel, small mol. Raf-1 kinase inhibitor,
BAY 43-9006, which belongs to a class that can be broadly described as bis-
aryl ureas. BAY 43-9006 was identified during a large medicinal chemical
optimization program, and this compound was selected for further pharmacol.
characterization based on its potent inhibition of Raf-1 (IC50 12 nM) and its
favorable kinase selectivity profile [2, 3]. In vitro and in vivo expts. were
designed to demonstrate effective blockade of the Raf/MEK/ERK signaling
pathway in tumor cells and for antitumor efficacy in human xenograft models.

IT 284461-73-0, BAY 43-9006

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor BAY 43-9006)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c
arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-0 (Pharmacology)

IT 284461-73-0, BAY 43-9006

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor BAY 43-9006)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS

L110 ANSWER 59 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:785444 HCAPLUS Full-text

DOCUMENT NUMBER: 137:362317

TITLE: BAY 43-9006: Early clinical data in patients with advanced solid malignancies

AUTHOR(S): Hotte, Sebastien J.; Hirte, Hal W.

CORPORATE SOURCE: Department of Medicine, Hamilton Regional Cancer Centre, McMaster University and Division of Medical Oncology, Hamilton, ON, Can.

SOURCE: Current Pharmaceutical Design (2002), 8(25), 2249-2253

CODEN: CPDEFP; ISSN: 1381-6128

PUBLISHER: Bentham Science Publishers

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Various signaling pathways can confer the malignant phenotype to a cell. Ras signaling proteins have been found to play an important role in controlling cellular growth. Raf-1 is a protein kinase that exerts its effects downstream of Ras in the mitogen-activated protein kinase pathway and is thus likely to be crucial in the development of the malignant phenotype. BAY 43-9006 is an orally administered selective inhibitor of Raf-1 and the first compound of its class to enter clin. trials. This article describes the early clin. data of BAY 43-9006 in patients with advanced, refractory solid tumors. To date, over 60 patients have been treated as part of four Phase I clin. trials. Dose levels have ranged from 50mg once weekly to 200mg twice-daily in continuous administration. The drug has been generally well tolerated with no dose limiting toxicity yet encountered. The more common toxicities have involved the gastrointestinal tract (diarrhea, nausea, abdominal cramping) and the skin (pruritus, rash, cheilitis). Pharmacokinetic evaluations have found BAY 43-9006 to have considerable interpatient variability. However, there seems to be an increase in Cmax and AUC values with increasing dose. There is no clear effect of food on bioavailability. Splitting the dose to twice-daily administration has shown increases in Cmax and AUC values but is also accompanied by considerable interpatient variability.

IT 475207-59-1, BAY 43-9006 mono-p-tosylate

RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(BAY 43-9006 for patients with advanced solid neoplasm)

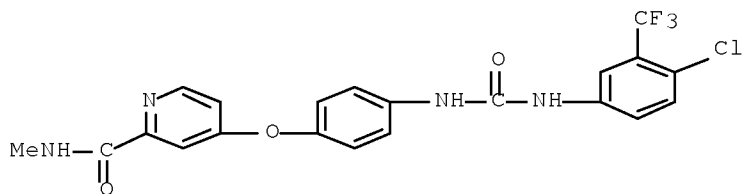
RN 475207-59-1 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl-, 4-methylbenzenesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 284461-73-0

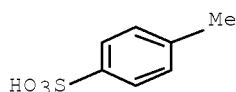
CMF C21 H16 Cl F3 N4 O3



CM 2

CRN 104-15-4

CMF C7 H8 O3 S



CC 1-0 (Pharmacology)

IT 475207-59-1, BAY 43-9006 mono-p-tosylate

RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(BAY 43-9006 for patients with advanced solid neoplasm)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 60 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:208292 HCAPLUS Full-text

DOCUMENT NUMBER: 139:269975

TITLE: Oncolytic Raf kinase inhibitor

AUTHOR(S): Sorbera, L. A.; Castaner, J.; Bozzo, J.; Leeson, P. A.

CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain

SOURCE: Drugs of the Future (2002), 27(12), 1141-1147

CODEN: DRFUD4; ISSN: 0377-8282

PUBLISHER: Prous Science

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with refs. The Ras/Raf/MEK pathway is a signaling module that controls cell growth and survival. Activation of this pathway results in a cascade of events from the cell surface to the nucleus ultimately affecting cellular proliferation, apoptosis, differentiation and transformation. Raf is a serine/threonine kinase that is a downstream effector enzyme of Ras. When activated, Raf goes on to activate MEK1 and MEK2 kinases which in turn phosphorylate and activate ERK1 and ERK2 which translocate to the nucleus where they stimulate pathways required for translation initiation and transcription activation leading to proliferation. Raf kinase has been validated as a potential and attractive target for hyperproliferative disorders such as cancer. Research has recently focused on efforts to discover potent Raf kinase inhibitors and several low-mol.-weight Raf kinase inhibitors have been described. Bis-aryl ureas were identified within this program using

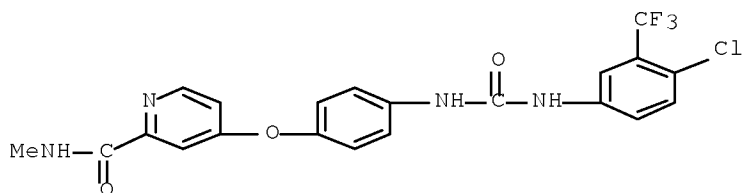
medicinal chemical-directed syntheses or combinatorial libraries. After high-throughput screening of more than 200,000 compds. against recombinant Raf-1 kinase, the orally active Bay-43-9006 was identified as having potent inhibitory activity and was chosen for further development as a treatment for cancer. Bay-43-9006 has exhibited potent in vitro activity against several tumor cell lines and has displayed efficacy in human tumor xenograft models. Moreover, results from phase I development in patients with a variety of cancer types indicates promising clin. efficacy for the compound

IT 284461-73-0, Bay-43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(oncolytic Raf kinase inhibitor)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c
arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-0 (Pharmacology)

IT 139691-76-2, Raf kinase 284461-73-0, Bay-43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(oncolytic Raf kinase inhibitor)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 61 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:493516 HCAPLUS Full-text

DOCUMENT NUMBER: 133:120157

TITLE: Preparation of ω-carboxy(hetero)aryl substituted
diphenyl ureas as raf kinase inhibitors

INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger,
Timothy B.; Scott, William J.; Smith, Roger A.; Wood,
Jill E.; Monahan, Mary-Katherine; Natero, Reina;
Renick, Joel; Sibley, Robert N.

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: PCT Int. Appl., 120 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|--------------|
| WO 2000042012 | A1 | 20000720 | WO 2000-US648 | 20000112 <-- |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, | | | | |

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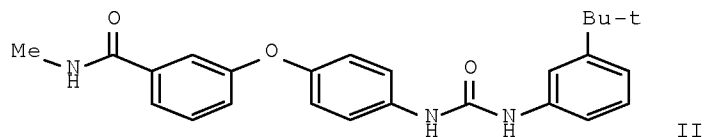
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| CA 2359510 | A1 | 20000720 | CA 2000-2359510 | 20000112 <-- |
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| EE 200100368 | A | 20030415 | EE 2001-368 | 20000112 <-- |
| EE 4913 | B1 | 20071015 | | |
| HU 2003000866 | A2 | 20030728 | HU 2003-866 | 20000112 <-- |
| HU 2003000866 | A3 | 20060428 | | |
| HU 225780 | B1 | 20070828 | | |
| JP 2003526613 | T | 20030909 | JP 2000-593580 | 20000112 <-- |
| JP 3845792 | B2 | 20061115 | | |
| BR 2000007487 | A | 20030923 | BR 2000-7487 | 20000112 <-- |
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| US 20010016659 | A1 | 20010823 | US 2001-773672 | 20010202 <-- |
| US 20010027202 | A1 | 20011004 | US 2001-773658 | 20010202 <-- |
| US 20010034447 | A1 | 20011025 | US 2001-773604 | 20010202 <-- |
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| MX 2001PA07118 | A | 20021023 | MX 2001-PA7118 | 20010712 <-- |
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| US 20020137774 | A1 | 20020926 | US 2001-907970 | 20010719 <-- |
| BG 105763 | A | 20020329 | BG 2001-105763 | 20010801 <-- |
| BG 65158 | B1 | 20070430 | | |
| BG 109688 | A | 20070531 | BG 2001-109688 | 20010801 <-- |
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| US 20030139605 | A1 | 20030724 | US 2002-71248 | 20020211 <-- |
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| AU 2004200722 | B2 | 20080110 | | |
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| JP 2006328075 | A | 20061207 | JP 2006-190034 | 20060711 <-- |
| KR 2007020158 | A | 20070216 | KR 2007-702656 | 20070201 <-- |
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| US 20080153823 | A1 | 20080626 | US 2007-956111 | 20071213 <-- |
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10/590724

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| US 1999-257266 | A2 19990225 <-- |
| US 1999-425228 | A2 19991022 <-- |
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| AU 2000-25016 | A3 20000112 <-- |
| CA 2000-2359510 | A3 20000112 <-- |
| CN 2000-802685 | A3 20000112 <-- |
| EP 2000-903239 | A3 20000112 <-- |
| JP 2000-593580 | A3 20000112 <-- |
| WO 2000-US648 | W 20000112 <-- |
| IN 2001-MN799 | A3 20010705 <-- |
| KR 2001-708847 | A3 20010712 <-- |
| US 2001-948915 | A1 20010910 <-- |
| US 2002-889227 | A1 20020108 <-- |

OTHER SOURCE(S): MARPAT 133:120157
GI



AB This invention relates to the preparation and use of (hetero)aryl ureas ANHCONHB [I; A = L(ML1)q; L = 5- or 6-membered (hetero)aryl, especially Ph or pyridinyl; M = bridging group; L1 = (hetero)aryl with at least one (un)substituted sulfamoyl, carboxy, or carbamoyl substituent; q = 1-3; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] for the treatment of raf mediated diseases, such as cancer (no data). Approx. 100 invention compds. and numerous intermediates were prepared For instance, 3-tert-butylaniline was coupled with bis(trichloromethyl)carbonate to form the isocyanate, followed by addition of 4-(3-N-methylcarbamoylphenoxy)aniline (preparation given) to afford the urea II.

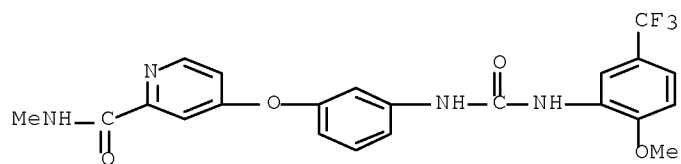
IT 284461-42-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of ω-carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)

RN 284461-42-3 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D211-78
ICS C07D211-72; A61K031-33; A61K031-54; A61K031-535; A61K031-17;
C07C275-20; C07C275-22; C07C275-24; C07C275-28

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1

IT 284461-33-2P, N-(3-tert-Butylphenyl)-N'-(4-(3-(N-methylcarbamoyl)phenoxy)phenyl)urea 284461-34-3P, N-(3-tert-Butylphenyl)-N'-(4-(4-acetylphenoxy)phenyl)urea 284461-36-5P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-[3-(N-methylcarbamoyl)phenoxy]phenyl]urea 284461-37-6P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-[4-methoxy-3-(N-methylcarbamoyl)phenoxy]phenyl]urea 284461-39-8P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-(1-oxoisindolin-5-yloxy)phenyl]urea 284461-42-3P 284461-43-4P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl]urea 284461-44-5P 284461-45-6P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridyloxy)phenyl]urea 284461-51-4P 284461-54-7P 284461-58-1P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[[2-(N-methylcarbamoyl)-4-pyridyl]thio]phenyl]urea 284461-74-1P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridyloxy)phenyl]urea 284461-75-2P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl]urea 284461-78-5P 284461-86-5P 284461-90-1P 284461-99-0P 284462-05-1P 284462-06-2P 284462-17-5P 284462-18-6P 284462-19-7P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[2-chloro-4-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea 284462-20-0P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[3-chloro-4-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea 284462-22-2P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[3-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea 284462-26-6P 284462-28-8P, N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[4-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea 284462-30-2P 284462-31-3P, N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[3-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea 284462-35-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of ω -carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)

IT 228418-48-2P 284461-35-4P 284461-40-1P 284461-41-2P 284461-46-7P 284461-47-8P 284461-49-0P 284461-50-3P 284461-52-5P 284461-53-6P 284461-55-8P 284461-56-9P 284461-57-0P 284461-59-2P 284461-60-5P 284461-61-6P 284461-62-7P 284461-63-8P 284461-64-9P 284461-65-0P 284461-66-1P 284461-67-2P 284461-68-3P 284461-69-4P 284461-70-7P 284461-71-8P 284461-72-9P 284461-77-4P 284461-79-6P 284461-80-9P 284461-81-0P 284461-82-1P 284461-83-2P 284461-84-3P 284461-85-4P 284461-88-7P 284461-91-2P 284461-92-3P 284461-93-4P 284461-94-5P 284461-95-6P 284461-96-7P 284461-97-8P 284461-98-9P 284462-00-6P 284462-01-7P 284462-02-8P 284462-03-9P 284462-04-0P 284462-07-3P 284462-08-4P 284462-09-5P 284462-10-8P 284462-11-9P 284462-12-0P 284462-13-1P 284462-15-3P 284462-16-4P 284462-21-1P 284462-23-3P 284462-24-4P 284462-25-5P 284462-27-7P 284462-32-4P 284462-33-5P 284462-34-6P 284462-36-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of ω -carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)

IT 98-98-6, Picolinic acid 99-98-9, 4-(Dimethylamino)aniline 106-50-3, p-Phenylenediamine, reactions 108-00-9, N,N-Dimethylethylenediamine 109-85-3, 2-Methoxyethylamine 110-13-4, Acetylacetone 123-30-8, 4-Aminophenol 320-51-4, 4-Chloro-3-(trifluoromethyl)aniline 327-78-6, 4-Chloro-3-(trifluoromethyl)phenyl isocyanate 349-65-5, 2-Methoxy-5-(trifluoromethyl)aniline 350-46-9, 1-Fluoro-4-nitrobenzene 371-40-4, 4-Fluoroaniline 393-36-2, 4-Bromo-3-(trifluoromethyl)aniline 462-08-8, 3-Aminopyridine 610-35-5, 4-Hydroxyphthalic acid 619-08-9, 2-Chloro-4-nitrophenol 626-61-9, 4-Chloropyridine 883-99-8, Methyl 3-hydroxy-2-naphthoate 1121-78-4, 5-Hydroxy-2-methylpyridine 1215-98-1, 4-(4-Acetylphenoxy)aniline 1664-40-0, N-Phenylethylenediamine 1877-71-0, Monomethyl isophthalate 2038-03-1, 4-(2-Aminoethyl)morpholine 2252-63-3, N-(4-Fluorophenyl)piperazine 2524-67-6, 4-Morpholinoaniline 2835-99-6, 4-Amino-3-methylphenol 2905-24-0, 3-Bromobenzenesulfonyl chloride 5369-19-7, 3-tert-Butylaniline 6310-19-6, 2-Nitro-4-tert-butylaniline 6628-77-9, 5-Amino-2-methoxypyridine 6927-86-2, 4-(4-Acetylphenoxy)aniline hydrochloride 7781-98-8, Ethyl 3-hydroxybenzoate 13154-24-0, Triisopropylsilyl chloride 16588-75-3 25900-61-2, 3-(Methylcarbamoyl)aniline 29264-35-5, 4-(3-Carboxy-4-hydroxyphenoxy)-1-nitrobenzene 30766-22-4, Methyl 5-hydroxynicotinate 30806-83-8, Ethyl 4-isocyanatobenzoate 34803-66-2, N-(2-Pyridyl)piperazine 36265-31-3, 4-(4-Methylthiophenoxy)-1-nitrobenzene 51639-48-6, N-(4-Acetylphenyl)piperazine 73441-86-8 150009-83-9, 3-Amino-2-methoxyquinoline 284461-38-7, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-(1,3-dioxoisindolin-5-yloxy)phenyl]urea 284461-48-9 284461-76-3, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(3-((2-(N-Methylcarbamoyl)-4-pyridyl)oxy)phenyl)urea 284462-29-9 284462-72-2, 3-Chloro-6-(N-acetylamino)-4-(trifluoromethyl)anisole 284462-73-3, 4-Chloro-N-(2-hydroxyethyl)pyridine-2-carboxamide 284462-74-4 284462-76-6 284462-77-7, 5-tert-Butyl-2-methoxyphenyl isocyanate 284462-78-8, 3-[[2-(N-Methylcarbamoyl)-4-pyridyl]oxy]aniline 284462-79-9, 3-(2-Carbamoyl-4-pyridyloxy)aniline 284462-80-2, 4-(2-Carbamoyl-4-pyridyloxy)aniline 284462-82-4, 4-[[2-(N-Ethylcarbamoyl)-4-pyridyl]oxy]aniline 284462-83-5, 4-[[2-(N-Methylcarbamoyl)-4-pyridyl]oxy]-3-chloroaniline 284462-85-7, 4-(3-Carbamoylphenoxy)aniline 284462-86-8, 4-[[2-(N,N-Dimethylcarbamoyl)-4-pyridyl]oxy]aniline 284462-87-9 284462-88-0 284462-89-1, 4-[[2-(N-Isopropylcarbamoyl)-4-pyridyl]oxy]aniline 284462-92-6, 3-[[2-(N-Methylcarbamoyl)-4-pyridyl]oxy]-4-methylaniline 284462-93-7, 4-[3-[N-(2-Morpholinylethyl)carbamoyl]phenoxy]aniline 284462-94-8, 4-[3-[N-(2-Piperidylethyl)carbamoyl]phenoxy]aniline 284462-95-9, 4-[3-[N-(Tetrahydrofurylmethyl)carbamoyl]phenoxy]aniline 284462-96-0 284462-99-3, 4-Chloro-2-methoxy-5-(trifluoromethyl)phenyl isocyanate 284670-99-1, 4-(4-Acetylphenoxy)-5-aminopyridine 284671-00-7, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-[4-[3-(5-methoxycarbonylpyridyl)oxy]phenyl]urea 284671-01-8, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-(3-carboxyphenyl)urea RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of ω -carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)

IT 883-62-5P, 3-Methoxy-2-naphthoic acid 13041-60-6P, Methyl 3-methoxy-2-naphthoate 27237-21-4P, 4-(3-Carboxyphenoxy)-1-nitrobenzene 36089-89-1P, 4-(4-Methylsulfonylphenoxy)-1-nitrobenzene 41513-02-4P, 4-Bromo-3-(trifluoromethyl)phenyl isocyanate 50727-06-5P, 5-Hydroxyisindoline-1,3-dione 51727-15-2P, 4-Chloropyridine-2-carbonyl chloride hydrochloride 54579-63-4P, 4-(3-Carboxyphenoxy)aniline

64064-63-7P, 4-[(2-Methylpyridin-5-yl)oxy]-1-nitrobenzene 67291-63-8P,
 2-Amino-3-methoxynaphthalene 71708-64-0P, 4-[3-(N-Methylcarbamoyl)phenoxy]-1-nitrobenzene 77992-50-8P,
 4-Bromo-3-(trifluoromethyl)aniline hydrochloride 119431-22-0P,
 3-Chloro-4-(2,2,2-trifluoroacetyl)amino)phenol 153435-79-1P,
 N-Methyl-3-bromobenzenesulfonamide 176977-85-8P, Methyl
 4-chloropyridine-2-carboxylate hydrochloride 220000-87-3P,
 4-Chloro-N-methyl-2-pyridinecarboxamide 228401-15-8P,
 2-(N-(Benzyloxycarbonyl)amino)-3-methoxynaphthalene 228401-43-2P,
 4-(3-Methoxycarbonyl-4-methoxyphenoxy)-1-nitrobenzene 228401-44-3P,
 4-(3-Carboxy-4-methoxyphenoxy)-1-nitrobenzene 252061-66-8P,
 5-Hydroxyisoindolin-1-one 284461-73-0P 284461-89-8P
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 284462-38-0P, 5-(4-Nitrophenoxy)isoindoline-1,3-dione 284462-39-1P,
 5-(4-Aminophenoxy)isoindoline-1,3-dione 284462-40-4P,
 1-(4-tert-Butyl-2-nitrophenyl)-2,5-dimethylpyrrole 284462-41-5P,
 5-tert-Butyl-2-(2,5-dimethylpyrrolyl)aniline 284462-42-6P,
 4-[[2-(N-Methylcarbamoyl)-4-pyridyl]oxy]-2-methylaniline hydrochloride
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(preparation of ω-carboxy(hetero)aryl substituted di-Ph urea raf
 kinase inhibitors by reacting arylisocyanates with arylamines)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 62 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:493376 HCAPLUS Full-text

DOCUMENT NUMBER: 133:120155

TITLE: Preparation of ω-carboxy aryl substituted
 diphenyl ureas as p38 kinase inhibitors

INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger,
 Timothy B.; Scott, William J.; Smith, Roger A.; Wood,
 Jill E.; Monahan, Mary-Katherine; Natero, Reina;
 Renick, Joel; Sibley, Robert N.

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: PCT Int. Appl., 148 pp.

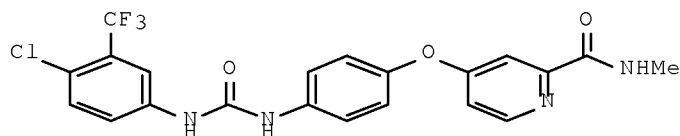
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-----------------|
| WO 2000041698 | A1 | 20000720 | WO 2000-US768 | 20000113 <-- |
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| US 20030139605 | A1 | 20030724 | US 2002-71248 | 20020211 <-- |
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| AU 2004200566 | A1 | 20040311 | AU 2004-200566 | 20040213 <-- |
| AU 2004200566 | B2 | 20060817 | | |
| AU 2004200722 | A1 | 20040318 | AU 2004-200722 | 20040224 <-- |
| AU 2004200722 | B2 | 20080110 | | |
| US 20080027061 | A1 | 20080131 | US 2007-845597 | 20070827 <-- |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 1999-115878P | P 19990113 <-- |
| | | | US 1999-257265 | A2 19990225 <-- |
| | | | US 1999-425229 | A2 19991022 <-- |
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| | | | US 1999-257266 | B2 19990225 <-- |
| | | | US 1999-425228 | B1 19991022 <-- |
| | | | AU 2000-25016 | A3 20000112 <-- |
| | | | AU 2000-27250 | A3 20000113 <-- |
| | | | WO 2000-US768 | W 20000113 <-- |
| | | | US 2001-948915 | A1 20010910 <-- |
| | | | US 2002-86417 | B3 20020304 <-- |
| OTHER SOURCE(S): MARPAT 133:120155 | | | | |
| GI | | | | |



II

AB The title compds. ADB [I; D = NHCONH; A = substituted moiety of up to 40 carbon atoms of the formula L(ML₁)_q (wherein L = 5-6 membered cyclic structure; L₁ = substituted cyclic moiety having at least 5 members; M = bridging group having at least one atom; q = 1-3; each of L and L₁ contains 0-4 members of the group consisting of N, O and S); B = (un)substituted up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the

group consisting of N, O and S], useful in treating p38 mediated diseases, were prepared E.g., a multi-step synthesis of the urea II which showed IC50 of 1-10 μ M against p38, was given. Compds. I are effective at 0.01-200 mg/kg/day (oral administration).

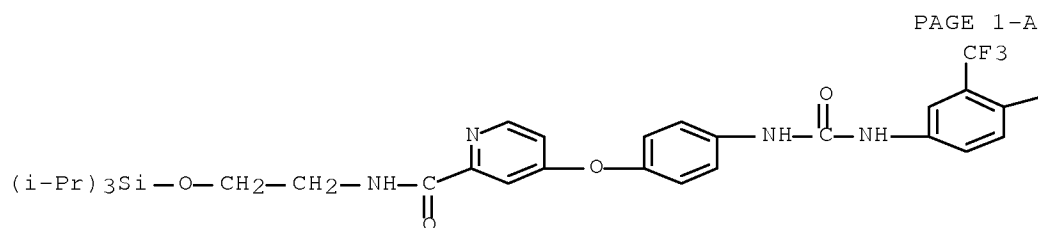
IT 284462-06-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of ω -carboxy aryl substituted di-Ph ureas as p38 kinase inhibitors)

RN 284462-06-2 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-[[tris(1-methylethyl)silyl]oxy]ethyl]- (CA INDEX NAME)



—Cl

IC ICM A61K031-535

ICS A61K031-50; A61K031-445; A61K031-44; A61K031-40; A61K031-34; A61K031-17

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1

IT 284461-86-5P 284461-89-8P 284462-06-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of ω -carboxy aryl substituted di-Ph ureas as p38 kinase inhibitors)

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| IT | 228418-48-2P | 284461-33-2P | 284461-34-3P | 284461-35-4P | 284461-36-5P |
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| | 284461-42-3P | 284461-43-4P | 284461-44-5P | | |
| | 284461-45-6P | 284461-46-7P | 284461-47-8P | | |
| | 284461-48-9P | 284461-49-0P | 284461-50-3P | | |
| | 284461-51-4P | 284461-52-5P | 284461-53-6P | 284461-54-7P | |
| | 284461-55-8P | 284461-56-9P | 284461-57-0P | 284461-58-1P | |
| | 284461-59-2P | 284461-60-5P | 284461-61-6P | 284461-62-7P | |
| | 284461-63-8P | 284461-64-9P | 284461-65-0P | 284461-66-1P | 284461-67-2P |
| | 284461-68-3P | 284461-69-4P | 284461-70-7P | 284461-71-8P | 284461-72-9P |

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284461-73-0P 284461-74-1P 284461-75-2P
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284462-70-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of ω -carboxy aryl substituted di-Ph ureas as p38 kinase inhibitors)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 63 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:421667 HCAPLUS Full-text

DOCUMENT NUMBER: 131:58659

TITLE: Preparation of diaryl ureas as inhibitors of p38 kinase.

INVENTOR(S): Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David; Hatoum-Mokdad, Holia; Rodriguez, Mareli; Sibley, Robert; Wang, Ming

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: PCT Int. Appl., 107 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|--|----------|-----------------|--------------|
| WO 9932463 | A1 | 19990701 | WO 1998-US27265 | 19981222 <-- |
| W: | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW | | | |
| RW: | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2315715 | A1 | 19990701 | CA 1998-2315715 | 19981222 <-- |
| AU 9919399 | A | 19990712 | AU 1999-19399 | 19981222 <-- |
| EP 1042305 | A1 | 20001011 | EP 1998-964221 | 19981222 <-- |
| EP 1042305 | B1 | 20050608 | | |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | |

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|--|----|----------|-----------------|-----------------|
| JP 2001526276 | T | 20011218 | JP 2000-525400 | 19981222 <-- |
| JP 3887769 | B2 | 20070228 | | |
| AT 297383 | T | 20050615 | AT 1998-964221 | 19981222 <-- |
| PT 1042305 | T | 20051031 | PT 1998-964221 | 19981222 <-- |
| ES 2154252 | T3 | 20051201 | ES 1998-964221 | 19981222 <-- |
| EP 1616865 | A1 | 20060118 | EP 2005-12144 | 19981222 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| MX 2000PA06227 | A | 20020311 | MX 2000-PA6227 | 20000622 <-- |
| HK 1032050 | A1 | 20051118 | HK 2001-102468 | 20010407 <-- |
| AU 2003213527 | A1 | 20030814 | AU 2003-213527 | 20030717 <-- |
| PRIORITY APPLN. INFO.: | | | US 1997-995749 | A 19971222 <-- |
| | | | AU 1999-19399 | A3 19981222 <-- |
| | | | EP 1998-964221 | A3 19981222 <-- |
| | | | WO 1998-US27265 | W 19981222 <-- |

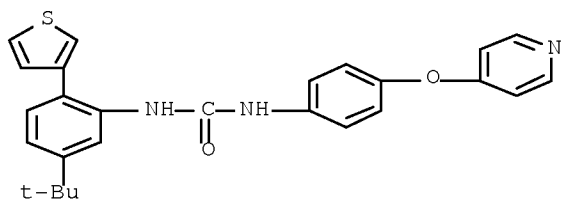
OTHER SOURCE(S): MARPAT 131:58659

AB A method of treating a p-38 mediated disease other than cancer comprises administration of BNHCONHA [A = (substituted) Ph, pyridyl, 2-thienyl; B = (substituted) aryl, heteroaryl containing ≥ 1 6-membered aromatic structure containing 0-4 N, O, or S atoms]. Thus, 5-tert-butyl-2-(3-tetrahydrofuranyloxy)aniline (preparation given) and p-tolyl isocyanate were stirred 8 h in PhMe to give 75% N-(5-tert-butyl-2-(3-tetrahydrofuranyloxy)phenyl)-N'-(4-methylphenyl)urea. Title compds. inhibited p38 kinase with IC₅₀ = 1-10 μ M.

IT 228399-44-8P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of diaryl ureas as inhibitors of p38 kinase)

RN 228399-44-8 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-(3-thienyl)phenyl]-N'-[4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME)



| | | | | |
|----|---|--------------|--------------|---------------------------|
| IC | ICM C07D273-00 | | | |
| | ICS C07D275-00; A61K031-17 | | | |
| CC | 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds) | | | |
| | Section cross-reference(s): 1, 27, 28 | | | |
| IT | 370-50-3P | 117745-34-3P | 228399-32-4P | 228399-33-5P 228399-34-6P |
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diaryl ureas as inhibitors of p38 kinase)

IT 228399-41-5 228418-48-2 228418-49-3

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of diaryl ureas as inhibitors of p38 kinase)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 64 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:421642 HCAPLUS Full-text

DOCUMENT NUMBER: 131:58658

TITLE: Inhibition of raf kinase using symmetrical and unsymmetrical substituted diphenyl ureas

INVENTOR(S): Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David; Rodriguez, Mareli; Wang, Ming

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: PCT Int. Appl., 89 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| ----- | --- | ----- | ----- | ----- |
| WO 9932436 | A1 | 19990701 | WO 1998-US26081 | 19981222 <-- |
| W: | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, | | | |

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TR, TT, UA, UG, UZ, VN, YU, ZW
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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| CA 2315646 | A1 | 19990701 | CA 1998-2315646 | 19981222 <-- |
| AU 9919054 | A | 19990712 | AU 1999-19054 | 19981222 <-- |
| AU 763024 | B2 | 20030710 | | |
| EP 1049664 | A1 | 20001108 | EP 1998-963809 | 19981222 <-- |
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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| TR 200002616 | T2 | 20001121 | TR 2000-2616 | 19981222 <-- |
| TR 200100874 | T2 | 20010621 | TR 2001-874 | 19981222 <-- |
| HU 2000004437 | A2 | 20010628 | HU 2000-4437 | 19981222 <-- |
| JP 2001526258 | T | 20011218 | JP 2000-525373 | 19981222 <-- |
| BR 9814375 | A | 20020521 | BR 1998-14375 | 19981222 <-- |
| NZ 505843 | A | 20030630 | NZ 1998-505843 | 19981222 <-- |
| EP 1449834 | A2 | 20040825 | EP 2003-26051 | 19981222 <-- |
| EP 1449834 | A3 | 20041222 | | |

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IE, SI, LT, LV, FI, RO, MK, CY, AL

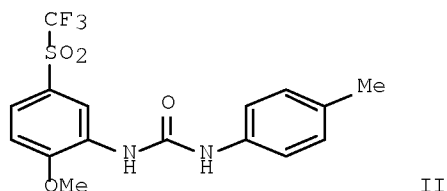
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| RU 2247109 | C2 | 20050227 | RU 2000-120165 | 19981222 <-- |
| AT 291011 | T | 20050415 | AT 1998-963809 | 19981222 <-- |
| ES 2153809 | T3 | 20050716 | ES 1998-963809 | 19981222 <-- |
| PL 195808 | B1 | 20071031 | PL 1998-342078 | 19981222 <-- |
| NO 2000003230 | A | 20000821 | NO 2000-3230 | 20000621 <-- |
| MX 2000PA06231 | A | 20020918 | MX 2000-PA6231 | 20000622 <-- |
| IN 2000MN00150 | A | 20050715 | IN 2000-MN150 | 20000704 <-- |
| BG 104599 | A | 20010330 | BG 2000-104599 | 20000712 <-- |
| BG 64594 | B1 | 20050831 | | |
| IN 2003MN00960 | A | 20050429 | IN 2003-MN960 | 20031013 <-- |

PRIORITY APPLN. INFO.:

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| US 1997-996344 | A | 19971222 <-- |
| EP 1998-963809 | A3 | 19981222 <-- |
| WO 1998-US26081 | W | 19981222 <-- |

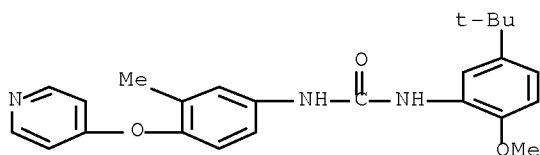
OTHER SOURCE(S): MARPAT 131:58658

GI



AB The invention relates to the use of a group of aryl ureas ANHCONHB [I; A = certain (un)substituted Ph, pyridinyl, or thien-2-yl groups; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] in treating raf-mediated diseases, and pharmaceutical compns. for use in such therapy. A subset of I are novel and are claimed per se. Approx. 160 invention compds. and numerous intermediates were prepared For instance, reaction of tolyl isocyanate with 2-methoxy-5-(trifluoromethanesulfonyl)aniline in EtOAc gave title compound II. In an in vitro raf kinase assay, all compds. displayed IC50 values between 1 nM and 10 µM.

IT 228399-40-4P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by raf kinase)
 RN 228399-40-4 HCAPLUS
 CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[3-methyl-4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME)



IC ICM C07C275-24
 ICS C07D213-02; C07D333-02; A61K031-17; A61K031-38; A61K031-44
 CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
 Section cross-reference(s): 1, 7
 IT 370-50-3P 228399-32-4P 228399-33-5P 228399-34-6P 228399-35-7P
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 228400-33-7P 228400-34-8P 228400-35-9P 228400-36-0P 228400-37-1P
 228400-38-2P 228400-39-3P 228400-40-6P 228400-41-7P 228400-42-8P
 228400-43-9P 228400-44-0P 228400-45-1P 228400-46-2P
 228400-47-3P 228400-48-4P 228400-49-5P 228400-50-8P
 228400-51-9P 228400-52-0P 228400-53-1P 228400-54-2P 228400-55-3P
 228400-56-4P 228400-57-5P 228400-58-6P 228400-60-0P
 228400-61-1P 228400-62-2P 228400-63-3P 228400-64-4P
 228400-65-5P 228400-66-6P 228400-67-7P 228400-69-9P 228400-70-2P
 228400-71-3P 228400-72-4P 228400-73-5P 228400-74-6P 228400-75-7P
 228400-76-8P 228400-77-9P 228400-78-0P
 228400-79-1P 228400-80-4P 228400-81-5P
 228400-82-6P 228400-83-7P 228400-84-8P
 228400-85-9P 228400-87-1P 228400-89-3P 228400-91-7P
 228400-92-8P 228400-93-9P 228400-94-0P 228400-95-1P 228400-96-2P
 228400-97-3P 228400-99-5P 228401-00-1P 228401-01-2P 228401-02-3P

10/590724

228401-03-4P 228401-04-5P 228401-06-7P 228401-07-8P 228401-49-8P
228401-50-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by raf kinase)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 65 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:591849 BIOSIS Full-text

DOCUMENT NUMBER: PREV200600585463

TITLE: Synthesis of iodine-123 labeled raf kinase inhibitor: A potential SPECT agent.

AUTHOR(S): Kabalka, George W. [Reprint Author]; Mereddy, Arjun R.; Schuller, Hildegard

CORPORATE SOURCE: Univ Tennessee, Dept Chem, Knoxville, TN 37996 USA
kabalka@utk.edu; amereddy@mc.utmck.edu

SOURCE: Abstracts of Papers American Chemical Society, (MAR 26 2006) Vol. 231, pp. 309-MEDI.
Meeting Info.: 231st National Meeting of the American-Chemical-Society. Atlanta, GA, USA. March 26 -30, 2006. Amer Chem Soc.
CODEN: ACSRAL. ISSN: 0065-7727.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 8 Nov 2006

Last Updated on STN: 8 Nov 2006

CC General biology - Symposia, transactions and proceedings 00520

Enzymes - General and comparative studies: coenzymes 10802

Pathology - Diagnostic 12504

Pathology - Therapy 12512

Respiratory system - Pathology 16006

Pharmacology - General 22002

Neoplasms - Diagnostic methods 24001

Neoplasms - Pathology, clinical aspects and systemic effects 24004

Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts

Pharmacology; Methods and Techniques; Tumor Biology; Enzymology
(Biochemistry and Molecular Biophysics)

IT Diseases

lung cancer: respiratory system disease, neoplastic disease, diagnosis, mortality

Lung Neoplasms (MeSH)

IT Chemicals & Biochemicals

BAY 43-9006: antineoplastic-drug, enzyme inhibitor-drug; iodine-123; raf kinase inhibitor; BAY 43-9006

radioiodinated analouge: antineoplastic-drug

IT Methods & Equipment

SPECT imaging [single photon emission computed tomography imaging]: laboratory techniques, diagnostic techniques, clinical techniques, imaging and microscopy techniques

GT USA (North America, Nearctic region)

RN 284461-73-0 (BAY 43-9006)

15715-08-9 (iodine-123)

L110 ANSWER 66 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN

ACCESSION NUMBER: 2006:663269 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600657401
TITLE: Sorafenib for the treatment of renal cell carcinoma.
AUTHOR(S): Hughes, Caren L. [Reprint Author]; Tan, Winston W.;
Ferrone, Marcus
CORPORATE SOURCE: Univ Texas, MD Anderson Canc Ctr, Div Pharm, Unit 90,1515
Holcombe Blvd, Houston, TX 77030 USA
calhughes@mdanderson.com
SOURCE: Journal of Pharmacy Technology, (SEP-OCT 2006) Vol. 22, No.
5, pp. 281-288.
CODEN: JPTEEB. ISSN: 8755-1225.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Nov 2006
Last Updated on STN: 29 Nov 2006

AB Objective: To summarize the pharmacology, development, and clinical application of sorafenib, a specific tyrosine kinase and vascular growth factor inhibitor, for the treatment of renal cell carcinoma (RCC).Data Sources: Clinical literature, including both primary studies and review articles, was obtained by searching MEDLINE (1966-May 2006), using the search terms BAY 43-9006, sorafenib, renal cell carcinoma, and tyrosine kinase inhibitor. Additional information was supplied by the manufacturer, Bayer HealthCare Pharmaceuticals.Study Selection and Data Extraction: Review articles, abstracts, and clinical studies related to sorafenib were analyzed. An evaluation of the research exploring sorafenib as a potential therapy for RCC was conducted. Relevant information was then selected and is reviewed in this article.Data Synthesis: Knowledge of the cellular abnormalities that can cause solid tumors has led to the development of medications that block these pathways. Sorafenib is an oral tyrosine kinase inhibitor that both blocks the Raf kinase pathway and inhibits vascular growth factors. Phase I and II trials have demonstrated that sorafenib has activity against RCC. Dermatologic reactions (rash, desquamation), fatigue, and hypertension have been the most commonly seen treatment-related adverse events. Sorafenib received FDA approval in December 2005 for treatment of advanced RCC.Conclusions: Sorafenib is a novel oral tyrosine kinase inhibitor effective in the treatment of RCC.

CC Cytology - Animal 02506
Cytology - Human 02508
Enzymes - General and comparative studies: coenzymes 10802
Pathology - Therapy 12512
Urinary system - Physiology and biochemistry 15504
Urinary system - Pathology 15506
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Toxicology - Pharmacology 22504
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts
Pharmacology; Oncology (Human Medicine, Medical Sciences); Urology
(Human Medicine, Medical Sciences)

IT Parts, Structures, & Systems of Organisms
renal cell: excretory system

IT Diseases
renal cell carcinoma: urologic disease, neoplastic disease, drug
therapy

Carcinoma, Renal Cell (MeSH); Kidney Neoplasms (MeSH)

IT Chemicals & Biochemicals
tyrosine kinase; vascular growth factor; BAY
43-9006: antineoplastic-drug; sorafenib: antineoplastic-drug, enzyme

inhibitor-drug, dosage, adverse effect, pharmacokinetics, Beyer
Healthcare Pharmaceuticals, phase II clinical trial, phase I clinical
trial

ORGN Classifier

Hominidae 86215

Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

human (common)

Taxa Notes

Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 80449-02-1 (tyrosine kinase)

284461-73-0 (BAY 43-9006)

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ACCESSION NUMBER: 2006:42184 BIOSIS Full-text

DOCUMENT NUMBER: PREV200600031990

TITLE: Targeted agents for the treatment of advanced renal cell
carcinoma.

AUTHOR(S): Stadler, Walter M. [Reprint Author]

CORPORATE SOURCE: Univ Chicago, Div Genitourinary Oncol, Hematol Oncol Sect,
Dept Med, Chicago, IL 60637 USA
wstadler@medicine.bsd.uchicago.edu

SOURCE: Cancer, (DEC 1 2005) Vol. 104, No. 11, pp. 2323-2333.
CODEN: CANCAR. ISSN: 0008-543X.

DOCUMENT TYPE: Article
General Review; (Literature Review)

LANGUAGE: English

ENTRY DATE: Entered STN: 28 Dec 2005

Last Updated on STN: 28 Dec 2005

AB Metastatic renal cell carcinoma (RCC) is currently one of the most treatment-resistant malignancies. However, the elucidation of the molecular mechanisms underlying RCC development has led to the identification of promising targets for novel therapeutic agents. The involvement of the Von Hippel-Lindau protein pathway in clear cell RCC suggests that downstream targets of this pathway, namely, signaling through vascular endothelial growth factor (VEGF) in endothelial cells, platelet-derived growth factor (PDGF) in endothelial cells and pericytes, and the epidermal growth factor receptor (EGFR) pathway in tumor cells are all reasonable and rational therapeutic targets. A number of agents are in development that target VEGF (bevacizumab, a recombinant, humanized monoclonal antibody) or its receptor, VEGFR (PTK787, SU011248, and BAY 43-9006, all of which are small molecule inhibitors). Agents targeting EGFR also are being investigated clinically (gefitinib, cetuximab, erlotinib, and ABX-EGF). The Raf/MEK/ERK pathway is an important downstream convergence point for signaling through VEGFR, platelet-derived growth factor receptor (PDGFR), and EGFR (all have receptor tyrosine kinase activity) and also has important antiapoptotic effects, thereby providing an attractive target for intervention. In addition to inhibiting VEGFR and PDGFR-mediated angiogenic pathways, BAY 43-9006 has been shown to inhibit the Raf/MEK/ERK pathway at the level of Raf kinase. MEK-directed therapeutic approaches are also in development. Given that multiple molecular pathways are implicated in tumor cell growth, antitumor activity may be increased by using individual agents that target multiple pathways, or by combining different agents to allow vertical or horizontal inhibition of relevant pathways.

CC Cytology - Animal 02506

Cytology - Human 02508

Biochemistry studies - Proteins, peptides and amino acids 10064

Enzymes - General and comparative studies: coenzymes 10802

Pathology - General 12502

Pathology - Therapy 12512
 Urinary system - Physiology and biochemistry 15504
 Urinary system - Pathology 15506
 Endocrine - General 17002
 Pharmacology - General 22002
 Pharmacology - Clinical pharmacology 22005
 Pharmacology - Urinary system 22032
 Neoplasms - Pathology, clinical aspects and systemic effects 24004
 Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts
 Pharmacology; Enzymology (Biochemistry and Molecular Biophysics);
 Oncology (Human Medicine, Medical Sciences); Nephrology (Human
 Medicine, Medical Sciences)

IT Parts, Structures, & Systems of Organisms
 renal cell: excretory system; endothelial cell: excretory system;
 pericyte: excretory system

IT Diseases
 metastatic renal cell carcinoma: urologic disease, neoplastic disease,
 drug therapy, pathology
 Carcinoma, Renal Cell (MeSH); Kidney Neoplasms (MeSH); Neoplasm
 Metastasis (MeSH)

IT Chemicals & Biochemicals
 Raf kinase [EC 2.7.1.37]; vascular endothelial
 growth factor [VEGF]; Raf; extracellular regulated kinase [ERK];
 mitogen activated protein kinase kinase [MEK] [EC 2.7.1.37];
 bevacizumab: antineoplastic-drug, renal-acting-drug; PTK787:
 antineoplastic-drug, renal-acting-drug; gefitinib: antineoplastic-drug,
 renal-acting-drug; cetuximab: antineoplastic-drug, renal-acting-drug;
 erlotinib: antineoplastic-drug, renal-acting-drug; platelet-derived
 growth factor receptor [PDGFR]: antiapoptotic effect; epidermal growth
 factor receptor [EGFR]: antiapoptotic effect; vascular endothelial
 growth factor receptor [VEGFR]: antiapoptotic effect; SU011248:
 antineoplastic-drug, renal-acting-drug; BAY 43-9006:
 antineoplastic-drug, renal-acting-drug, enzyme inhibitor-drug;
 ABX-epidermal growth factor receptor [ABX-EGF]: antineoplastic-drug,
 renal-acting-drug

IT Miscellaneous Descriptors
 angiogenesis

ORGN Classifier
 Hominidae 86215
 Super Taxa
 Primates; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 human (common)
 Taxa Notes
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 144378-33-6 (Raf kinase)
 144378-33-6 (EC 2.7.1.37)
 127464-60-2 (vascular endothelial growth factor)
 127464-60-2 (VEGF)
 142805-58-1 (mitogen activated protein kinase kinase)
 142805-58-1 (MEK)
 142805-58-1 (EC 2.7.1.37)
 216974-75-3 (bevacizumab)
 212142-18-2 (PTK787)
 184475-35-2 (gefitinib)
 205923-56-4 (cetuximab)
 183321-74-6 (erlotinib)
 284461-73-0 (BAY 43-9006)

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ACCESSION NUMBER: 2007:264012 BIOSIS Full-text
DOCUMENT NUMBER: PREV200700274079
TITLE: BAY 43-9006 (sorafenib) is a potent inhibitor of FLT3
tyrosine kinase signaling and
proliferation in AML cells.
AUTHOR(S): Auclair, Daniel [Reprint Author]; Miller, Donna; Carter,
Christopher; Chang, Yong; Polony, Barbara; Zhang, Xiaomei;
Yatsula, Victoria; Pickett, Walter; Housley, Timothy; Burd,
Amy; Shi, Hong; Rocks, Sandy; Gedrich, Richard; Abriola,
Laura; Apanovitch, Don; Enyedy, Istvan; Dumas, Jacques;
Riedl, Bernd; Trail, Pamela A.; Wilhelm, Scott M.
CORPORATE SOURCE: Bayer Healthcare Pharmaceut, West Haven, CT USA
SOURCE: Proceedings of the American Association for Cancer Research
Annual Meeting, (APR 2005) Vol. 46, pp. 1409.
Meeting Info.: 96th Annual Meeting of the
American-Association-for-Cancer-Research. Anaheim, CA, USA.
April 16 -20, 2005. Amer Assoc Canc Res.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Apr 2007
Last Updated on STN: 11 Jul 2007
CC General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Cytology - Human 02508
Enzymes - General and comparative studies: coenzymes 10802
Pathology - Therapy 12512
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008
Neoplasms - Blood and reticuloendothelial neoplasms 24010
IT Major Concepts
Pharmacology; Blood and Lymphatics (Transport and Circulation);
Enzymology (Biochemistry and Molecular Biophysics); Tumor Biology
IT Parts, Structures, & Systems of Organisms
blood: blood and lymphatics
IT Diseases
acute myeloid leukemia: neoplastic disease, blood and lymphatic disease
Leukemia, Myeloid (MeSH)
IT Chemicals & Biochemicals
ERK1/2; Stat5; RAF kinase; VEGFR [vascular
endothelial growth factor receptor]; FLT3 tyrosine
kinase: signaling; BAY 43-9006 [Sorafenib]:
antineoplastic-drug, enzyme inhibitor-drug
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
MV4-11 cell line (cell_line)
HEK-293 cell line (cell_line)
RS4-11 cell line (cell_line)
EOL-1 cell line (cell_line)

Taxa Notes
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier
 Muridae 86375

Super Taxa
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia

Organism Name
 mouse (common)

Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN 144378-33-6 (RAF kinase)
 284461-73-0 (BAY 43-9006)
 284461-73-0 (Sorafenib)

L110 ANSWER 69 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:258211 BIOSIS Full-text

DOCUMENT NUMBER: PREV200510048678

TITLE: Raf kinase as a target for anticancer therapeutics.

AUTHOR(S): Sridhar, Srikala S.; Hedley, David; Siu, Lillian L.
 [Reprint Author]

CORPORATE SOURCE: Univ Hlth Network, Princess Margaret Hosp, Dept Med Oncol and Hematol, 610 Univ Ave, Suite 5-210, Toronto, ON M5G 2M9, Canada
 lillian.siu@uhn.on.ca

SOURCE: Molecular Cancer Therapeutics, (APR 2005) Vol. 4, No. 4, pp. 677-685.
 ISSN: 1535-7163.

DOCUMENT TYPE: Article
 General Review; (Literature Review)

LANGUAGE: English

ENTRY DATE: Entered STN: 14 Jul 2005
 Last Updated on STN: 14 Jul 2005

AB The Ras-Raf-MEK-ERK (ERK) pathway is a logical therapeutic target because it represents a common downstream pathway for several key growth factor tyrosine kinase receptors, which are often mutated or overexpressed in human cancers. Although considered mainly growth-promoting, in certain contexts, this pathway also seems to be apoptosis-suppressing. Several novel agents targeting this pathway have now been developed and are in clinical trials. One of the most interesting new agents is BAY 43-9006. Although initially developed as a Raf kinase inhibitor, it can also target several other important tyrosine kinases including VEGFR-2, Flt-3, and c-Kit, which contributes to its antiproliferative and antiangiogenic properties. To date, encouraging results have been seen with BAY 43-9006, particularly in renal cell cancers which are highly vascular tumors. This review will provide an overview of the ERK signaling pathway in normal and neoplastic tissue, with a specific focus on novel therapies targeting the ERK pathway at the level of Raf kinase.

CC Pathology - Therapy 12512
 Urinary system - Pathology 15506
 Pharmacology - General 22002
 Pharmacology - Clinical pharmacology 22005
 Neoplasms - Pathology, clinical aspects and systemic effects 24004
 Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts
 Pharmacology; Oncology (Human Medicine, Medical Sciences); Urology (Human Medicine, Medical Sciences)

IT Diseases
 renal cancer: urologic disease, neoplastic disease, drug therapy

Kidney Neoplasms (MeSH)

IT Chemicals & Biochemicals
 Raf kinase [EC 2.7.1.37]; BAY 43-9006:
 antineoplastic-drug, enzyme inhibitor-drug; VEGFR-2 kinase; Fit-3
 kinase; c-Kit kinase

ORGN Classifier
 Hominidae 86215
 Super Taxa
 Primates; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 human (common)
 Taxa Notes
 Animals, Chordates, Humans, Mammals, Primates, Vertebrate

RN 144378-33-6 (Raf kinase)
 144378-33-6 (EC 2.7.1.37)
 284461-73-0 (BAY 43-9006)
 218925-58-7 (VEGFR-2 kinase)
 138359-29-2 (c-Kit kinase)

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ACCESSION NUMBER: 2005:185218 BIOSIS Full-text
 DOCUMENT NUMBER: PREV200500186216
 TITLE: The Raf kinase inhibitor BAY
 43-9006 reduces cellular uptake of platinum compounds and
 cytotoxicity in human colorectal carcinoma cell lines.

AUTHOR(S): Heim, Martina; Scharifi, Mariam; Zisowsky, Jochen; Jaehde,
 Ulrich; Voliotis, Dimitris; Seeber, Siegfried; Strumberg,
 Dirk [Reprint Author]

CORPORATE SOURCE: Sch MedDept Hematol and Med Oncol, Ruhr Univ Bochum,
 Holkeskampring 40, D-44621, Herne, Germany
 dirk.strumberg@uni-essen.de

SOURCE: Anti-Cancer Drugs, (February 2005) Vol. 16, No. 2, pp.
 129-136. print.
 CODEN: ANTDEV. ISSN: 0959-4973.

DOCUMENT TYPE: Article
 LANGUAGE: English
 ENTRY DATE: Entered STN: 18 May 2005
 Last Updated on STN: 18 May 2005

AB Raf kinase plays a central role in oncogenic signaling and acts as a
 downstream effector of Ras in the extracellular signal-regulated (ERK) kinase
 pathway. BAY 43-9006 (BAY) is a novel signal transduction inhibitor that
 prevents tumor cell proliferation and angiogenesis through blockade of the
 Raf/MEK/ERK pathway at the level of Raf kinase and the receptor tyrosine
 kinases vascular endothelial growth factor receptor-2 and platelet-derived
 growth factor receptor-beta. The present study evaluates the effects of
 combining BAY and platinum derivatives on human colorectal cancer cells using
 different incubation protocols. Our data show that the combination of
 oxaliplatin or cisplatin with BAY results in marked antagonism irrespective of
 the used application schedule. Furthermore, BAY abrogates the cisplatin-
 induced G2 arrest as well as the G1 arrest induced by oxaliplatin. BAY alone
 arrests cancer cells in their current cell cycle phase and affects cell cycle
 regulative genes. Specifically, BAY reduced the protein expression of p21Cip1
 as well as cyclin D1, and inhibits the expression of cdc2 (cdk1). Utilizing
 atom absorption spectrometry, BAY significantly reduced cellular uptake of
 platinum compounds and thereby the generation of DNA adducts. Taken together,
 co-incubation with BAY results in reduced cellular uptake of platinum
 compounds and consecutively reduced generation of DNA adducts, and eventually
 decreased cellular cytotoxicity in human colorectal cancer cells. Our results
 indicate that the Raf kinase inhibitor BAY 43-9006 might also directly or

indirectly interact with platinum transporter proteins in vitro. Copyright
2005 Lippincott Williams & Wilkins.

CC Genetics - General 03502
Genetics - Human 03508
Biochemistry studies - General 10060
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Minerals 10069
Enzymes - General and comparative studies: coenzymes 10802
Pathology - Therapy 12512
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics);
Pharmacology; Tumor Biology

IT Chemicals & Biochemicals
BAY 43-9006: antineoplastic-drug, enzyme inhibitor-drug; DNA; Mek;
Raf kinase [EC 2.7.1.37]; cdc2; cisplatin:
antineoplastic-drug; cyclin D1; extracellular signal-regulated kinase
[EC 2.7.1.37]; oxaliplatin: antineoplastic-drug; p21Cip1;
platelet-derived growth factor receptor-beta; platinum; vascular
endothelial growth factor receptor-2

IT Methods & Equipment
atom absorption spectrometry: laboratory techniques, spectrum analysis
techniques

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
HCT8 cell line (cell line): human colon carcinoma cells
HT 29 cell line (cell line): human colon carcinoma cells
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 284461-73-0 (BAY 43-9006)
144378-33-6 (Raf kinase)
9026-43-1 (Raf kinase)
144378-33-6 (EC 2.7.1.37)
9026-43-1 (EC 2.7.1.37)
15663-27-1 (cisplatin)
142243-02-5 (extracellular signal-regulated kinase)
9026-43-1 (extracellular signal-regulated kinase)
142243-02-5 (EC 2.7.1.37)
9026-43-1 (EC 2.7.1.37)
61825-94-3 (oxaliplatin)
7440-06-4 (platinum)

L110 ANSWER 71 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
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ACCESSION NUMBER: 2005:32325 BIOSIS Full-text
DOCUMENT NUMBER: PREV200500030385
TITLE: BAY 43-9006 exhibits broad spectrum oral antitumor activity
and targets the RAF/MEK/ERK pathway and receptor
tyrosine kinases involved in tumor
progression and angiogenesis.
AUTHOR(S): Wilhelm, Scott M. [Reprint Author]; Carter, Christopher;
Tang, Liya; Wilkie, Dean; McNabola, Angela; Rong, Hong;
Chen, Charles; Zhang, Xiaomei; Vincent, Patrick; McHugh,

10/590724

Mark; Cao, Yichen; Shujath, Jaleel; Gawlak, Susan;
Eveleigh, Deepa; Rowley, Bruce; Liu, Li; Adnane, Lila;
Lynch, Mark; Auclair, Daniel; Taylor, Ian; Gedrich, Rich;
Voznesensky, Andrei; Riedl, Bernd; Post, Leonard E.;
Bollag, Gideon; Trail, Pamela A.

CORPORATE SOURCE: Dept Canc Res, Bayer Pharmaceut Corp, 400 Morgan Lane, W
Haven, CT, 06516, USA

scott.wilhelm.b@bayer.com

SOURCE: Cancer Research, (October 1 2004) Vol. 64, No. 19, pp.
7099-7109. print.

ISSN: 0008-5472 (ISSN print).

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 12 Jan 2005

Last Updated on STN: 12 Jan 2005

AB The RAS/RAF signaling pathway is an important mediator of tumor cell proliferation and angiogenesis. The novel bi-aryl urea BAY 43-9006 is a potent inhibitor of Raf-1, a member of the RAF/MEK/ERK signaling pathway. Additional characterization showed that BAY 43-9006 suppresses both wild-type and V599E mutant BRAF activity in vitro. In addition, BAY 43-9006 demonstrated significant activity against several receptor tyrosine kinases involved in neovascularization and tumor progression, including vascular endothelial growth factor receptor (VEGFR)-2, VEGFR-3, platelet-derived growth factor receptor beta, Fit-3, and c-KIT. In cellular mechanistic assays, BAY 43-9006 demonstrated inhibition of the mitogen-activated protein kinase pathway in colon, pancreatic, and breast tumor cell lines expressing mutant KRAS or wild-type or mutant BRAF, whereas non-small-cell lung cancer cell lines expressing mutant KRAS were insensitive to inhibition of the mitogen-activated protein kinase pathway by BAY 43-9006. Potent inhibition of VEGFR-2, platelet-derived growth factor receptor P, and VEGFR-3 cellular receptor autophosphorylation was also observed for BAY 43-9006. Once daily oral dosing of BAY 43-9006 demonstrated broad-spectrum antitumor activity in colon, breast, and non-small-cell lung cancer xenograft models. Immunohistochemistry demonstrated a close association between inhibition of tumor growth and inhibition of the extracellular signal-regulated kinases (ERKs) 1/2 phosphorylation in two of three xenograft models examined, consistent with inhibition of the RAF/MEK/ERK pathway in some but not all models. Additional analyses of microvessel density and microvessel area in the same tumor sections using antimurine CD31 antibodies demonstrated significant inhibition of neovascularization in all three of the xenograft models. These data demonstrate that BAY 43-9006 is a novel dual action RAF kinase and VEGFR inhibitor that targets tumor cell proliferation and tumor angiogenesis.

CC Cytology - General 02502
Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Digestive system - Pathology 14006
Respiratory system - Pathology 16006
Reproductive system - Pathology 16506
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Oncology (Human
Medicine, Medical Sciences); Pharmacology

IT Diseases
breast cancer: neoplastic disease, reproductive system disease/female

Breast Neoplasms (MeSH)

IT Diseases
colon cancer: digestive system disease, neoplastic disease
Colonic Neoplasms (MeSH)

IT Diseases
non-small-cell lung cancer: neoplastic disease, respiratory system disease
Carcinoma, Non-Small-Cell Lung (MeSH); Lung Neoplasms (MeSH)

IT Diseases
pancreatic cancer: digestive system disease, neoplastic disease
Pancreatic Neoplasms (MeSH)

IT Chemicals & Biochemicals
BRAF protein; Bay 43-9006: antineoplastic-drug, oral administration;
CD31 antibody; Flt-3; MEK/ERK; RAF; RAS; Raf-1 [EC 2.7.1.37]; c-KIT;
mitogen-activated protein kinase pathway; platelet-derived growth factor receptor beta; receptor tyrosine kinase [EC 2.7.1.112]; vascular endothelial growth factor receptor 2 [VEGFR-2]; vascular endothelial growth factor receptor 3 [VEGFR-3]

IT Methods & Equipment
cellular mechanistic assay: bioassay techniques, laboratory techniques;
immunochemistry: immunologic techniques, laboratory techniques

IT Miscellaneous Descriptors
RAF/MEK/ERK signaling pathway; angiogenesis; tumor progression

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
BxPC-3 cell line (cell line)
HASMC cell line (cell line)
HEK-293 cell line (cell line)
HUVEC cell line (cell line)
LOX cell line (cell line)
MDA-MB-231 cell line (cell line)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
NIH 3T3 cell line (cell line)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN 284461-73-0 (Bay 43-9006)
9026-43-1 (Raf-1)
9026-43-1 (EC 2.7.1.37)
340830-03-7 (receptor tyrosine kinase)
80449-02-1 (receptor tyrosine kinase)
340830-03-7 (EC 2.7.1.112)
80449-02-1 (EC 2.7.1.112)

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ACCESSION NUMBER: 2004:391335 BIOSIS Full-text

DOCUMENT NUMBER: PREV200400393629

TITLE: Validation of a liquid chromatography assay for the quantification of the Raf kinase inhibitor BAY 43-9006 in small volumes of mouse

serum.

AUTHOR(S): Afify, Samar; Rapp, Ulf R.; Hogger, Petra [Reprint Author]

CORPORATE SOURCE: Inst Pharm and Lebensmittelchem, Univ Wurzburg, Am Hubland, D-97074, Wurzburg, Germany
hogger@pzh.uni-wuerzburg.de

SOURCE: Journal of Chromatography B, (September 25 2004) Vol. 809, No. 1, pp. 99-103. print.
ISSN: 1570-0232 (ISSN print).

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 6 Oct 2004
Last Updated on STN: 6 Oct 2004

AB BAY 43-9006 is a selective Raf-1 kinase inhibitor with antitumor activity against a variety of human cancers. A highly sensitive HPLC method for determination of BAY 43-9006 in small volumes of serum (30 µl) was developed. Sample preparation involved a liquid-liquid extraction procedure with tolinaftate as internal standard followed by linear gradient elution at a reversed phase C18 column and UV detection. The method was selective and the calibration curves were linear over the concentration range of 80-2000 ng/ml. The intra-day accuracy ranged from 99.9 to 107.6% and the inter-day accuracy from 94.6 to 115%. The lower limit of quantitation (LOQ) was 80 ng/ml with an accuracy of 105.8%. Thus, this method has been validated and can be applied for the drug monitoring or pharmacokinetic studies of BAY 43-9006 in small volumes of serum samples. Copyright 2004 Elsevier B.V. All rights reserved.

CC Pathology - Therapy 12512
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts
Methods and Techniques; Pharmacology

IT Parts, Structures, & Systems of Organisms
serum: blood and lymphatics, small volumes

IT Diseases
cancer: neoplastic disease, drug therapy
Neoplasms (MeSH)

IT Chemicals & Biochemicals
BAY 43-9006: antineoplastic-drug, enzyme inhibitor-drug, selective
Raf-1 kinase inhibitor; tolinaftate: internal standard

IT Methods & Equipment
UV detection: laboratory techniques, spectrum analysis techniques;
linear gradient elution: laboratory techniques; liquid chromatography:
chromatographic techniques, laboratory techniques; liquid-liquid
extraction: laboratory techniques; reversed phase C-18 column:
laboratory equipment

IT Miscellaneous Descriptors
calibration curves; inter-day accuracy; intra-day accuracy; lower limit
of quantitation [LOQ]

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse (common)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
Rodents, Vertebrates

RN 284461-73-0 (BAY 43-9006)
2398-96-1 (tolinaftate)

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ACCESSION NUMBER: 2003189385 EMBASE Full-text
 TITLE: Clinical review 158 - Beyond radioiodine: A review of potential new therapeutic approaches for thyroid cancer.
 AUTHOR: Braga-Basaria, Milena; Ringel, Matthew D., Dr. (correspondence)
 CORPORATE SOURCE: Washington Hospital Center, MedStar Research Institute, Washington, DC 20010, United States. matthew.ringel@medstar.net
 AUTHOR: Braga-Basaria, Milena
 CORPORATE SOURCE: SEMPR, Servico de Endocrinol. e Metabologia, Univ. Federal do Parana, Curitiba 80.060-240, Brazil.
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 AUTHOR: Ringel, Matthew D., Dr. (correspondence)
 CORPORATE SOURCE: 110 Irving Street NW, Washington, DC 20010, United States. matthew.ringel@medstar.net
 SOURCE: Journal of Clinical Endocrinology and Metabolism, (1 May 2003) Vol. 88, No. 5, pp. 1947-1960.
 Refs: 104
 ISSN: 0021-972X CODEN: JCEMAZ
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 016 Cancer
 003 Endocrinology
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 29 May 2003
 Last Updated on STN: 29 May 2003

AB One of the greatest challenges in the management of patients with follicular cell-derived thyroid cancer is the treatment of tumors that progress despite surgery, radioiodine, and T(4) suppression of TSH. As knowledge of thyroid cancer biology improves, the potential exists to develop compounds targeted to treat thyroid cancers that do not respond to traditional therapy. Recently, the development of therapies targeted against specific molecular pathways involved in cancer progression has resulted in dramatic responses in patients with chronic myelogenous leukemia, gastrointestinal stromal tumors, and other cancers. A number of compounds are currently being evaluated in clinical trials that alter pathways involved thyroid cancer, and several of these agents have been tested in thyroid cancer in vitro and in vivo. In this review we will discuss the mechanisms of action and preclinical/clinical data for several of these compounds that have the potential to play an important role in the management of thyroid cancer in the future.

CT Medical Descriptors:
 breast carcinoma: DT, drug therapy
 cancer radiotherapy
 clinical trial
 colon carcinoma: DT, drug therapy
 colorectal carcinoma: DT, drug therapy
 drug activity
 drug effect
 drug receptor binding
 gene activation
 gene function

gene mutation
 head and neck carcinoma: DT, drug therapy
 head and neck carcinoma: RT, radiotherapy
 hematologic malignancy: DT, drug therapy
 human
 lung carcinoma: DT, drug therapy
 nonhuman
 pancreas carcinoma: DT, drug therapy
 priority journal
 prostate carcinoma: DT, drug therapy
 protein expression
 review
 side effect: SI, side effect
 solid tumor: DT, drug therapy
 *thyroid carcinoma: DT, drug therapy
 *thyroid carcinoma: ET, etiology
 urinary tract carcinoma: DT, drug therapy

CT

Drug Descriptors:
 2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: AE, adverse drug reaction
 2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: CT, clinical trial
 2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: DT, drug therapy
 2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: PO, oral drug administration
 3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: CT, clinical trial
 3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: CB, drug combination
 3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: DT, drug therapy
 3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: PD, pharmacology
 *antisense oligonucleotide: AE, adverse drug reaction
 *antisense oligonucleotide: CT, clinical trial
 *antisense oligonucleotide: CB, drug combination
 *antisense oligonucleotide: DT, drug therapy
 *antisense oligonucleotide: PD, pharmacology
 bevacizumab: AE, adverse drug reaction
 bevacizumab: CT, clinical trial
 bevacizumab: DT, drug therapy
 bevacizumab: PD, pharmacology
 cgp 69846a: AE, adverse drug reaction
 cgp 69846a: CT, clinical trial
 cgp 69846a: DT, drug therapy
 cgp 69846a: PD, pharmacology
 cisplatin: CB, drug combination
 cisplatin: DT, drug therapy
 doxorubicin: CB, drug combination
 doxorubicin: DT, drug therapy
 epidermal growth factor receptor: EC, endogenous compound
 epidermal growth factor receptor antibody: CT, clinical trial
 epidermal growth factor receptor antibody: DT, drug therapy
 epidermal growth factor receptor antibody: PD, pharmacology
 gemcitabine: CB, drug combination
 gemcitabine: DT, drug therapy
 isis 2503: AE, adverse drug reaction
 isis 2503: CT, clinical trial
 isis 2503: CB, drug combination

isis 2503: DT, drug therapy
 isis 2503: PD, pharmacology
 l 778123: AE, adverse drug reaction
 l 778123: CT, clinical trial
 lonafarnib: AE, adverse drug reaction
 lonafarnib: CT, clinical trial
 lonafarnib: CB, drug combination
 lonafarnib: DT, drug therapy
 manumycin: CB, drug combination
 manumycin: DT, drug therapy
 manumycin: PD, pharmacology
 mitogen activated protein kinase inhibitor: AE, adverse drug reaction
 mitogen activated protein kinase inhibitor: CT, clinical trial
 mitogen activated protein kinase inhibitor: DT, drug therapy
 mitogen activated protein kinase inhibitor: PO, oral drug administration
 paclitaxel: CB, drug combination
 paclitaxel: DT, drug therapy
 paclitaxel: PD, pharmacology
 phenylacetic acid: AE, adverse drug reaction
 phenylacetic acid: CT, clinical trial
 phenylacetic acid: IV, intravenous drug administration
 phenylacetic acid: PD, pharmacology
 phosphotransferase inhibitor: AE, adverse drug reaction
 phosphotransferase inhibitor: CT, clinical trial
 phosphotransferase inhibitor: DT, drug therapy
 phosphotransferase inhibitor: PD, pharmacology
 protein antibody
 protein farnesyltransferase inhibitor: CT, clinical trial
 *radioactive iodine: DT, drug therapy
 Ras protein: EC, endogenous compound
 semaxanib: DT, drug therapy
 semaxanib: PD, pharmacology
 sorafenib
 tipifarnib: CT, clinical trial
 tipifarnib: CB, drug combination
 tipifarnib: DT, drug therapy
 topotecan: CB, drug combination
 topotecan: DT, drug therapy
 trastuzumab: CT, clinical trial
 trastuzumab: CB, drug combination
 trastuzumab: DT, drug therapy
 trastuzumab: PD, pharmacology
 tyrosine kinase receptor: EC, endogenous compound

unindexed drug
 vasculotropin antibody: AE, adverse drug reaction
 vasculotropin antibody: CT, clinical trial
 vasculotropin antibody: DT, drug therapy
 vasculotropin antibody: PD, pharmacology
 vasculotropin receptor: EC, endogenous compound
 RN (2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide)
 212631-79-3; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4
 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9,
 195987-41-8; (bevacizumab) 216974-75-3; (cgp 69846a) 177075-18-2;
 (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (doxorubicin) 23214-92-8,
 25316-40-9; (gemcitabine) 103882-84-4; (isis 2503) 149957-14-2;
 (lonafarnib) 193275-84-2; (manumycin) 52665-74-4; (paclitaxel) 33069-62-4;
 (phenylacetic acid) 103-82-2; (semaxanib) 186610-95-7; (sorafenib)
 284461-73-0; (tipifarnib) 192185-72-1; (topotecan) 119413-54-6,
 123948-87-8; (trastuzumab) 180288-69-1; (vasculotropin receptor)
 301253-48-5

CN (1) avastin; (2) isis 2503; (3) isis 5132; (4) 1 778123; (5) lonafarnib;
 (6) semaxanib; (7) tipifarnib; (8) trastuzumab; bay 439006; bms 214662; pd
 184352

CO (1) Genentech (United States); (2) Isis (United States); (3) Isis; (4)
 Merck and Co (United States); (5) Schering Plough (United States); (6)
 Sugen (United States); (7) Johnson and Johnson (United States); (8)
 Genentech

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ACCESSION NUMBER: 2003455328 EMBASE Full-text
 TITLE: Tyrosine Kinase Inhibitors as Cancer
 Therapy.
 AUTHOR: Nichols, Gwen L., Dr. (correspondence)
 CORPORATE SOURCE: Department of Medicine, Division of Hematology, Columbia
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 CORPORATE SOURCE: 650 W. 168th St., New York, NY 10032, United States.
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 SOURCE: Cancer Investigation, (2003) Vol. 21, No. 5, pp. 758-771.
 Refs: 108
 ISSN: 0735-7907 CODEN: CINVD7
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 016 Cancer
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 LANGUAGE: English
 ENTRY DATE: Entered STN: 11 Dec 2003
 Last Updated on STN: 11 Dec 2003

CT Medical Descriptors:
 autocrine effect
 breast cancer: DT, drug therapy
 *cancer therapy
 clinical trial
 colorectal cancer: DT, drug therapy
 enzyme activation
 enzyme inhibition
 gene mutation
 gene overexpression
 gene translocation
 human
 kidney carcinoma: DT, drug therapy
 lung non small cell cancer: DT, drug therapy
 lung small cell cancer: DT, drug therapy
 melanoma: DT, drug therapy
 mesothelioma: DT, drug therapy
 meta analysis
 ovary cancer: DT, drug therapy
 paracrine signaling
 phase 1 clinical trial
 phase 2 clinical trial
 phase 3 clinical trial
 priority journal
 review
 signal transduction

CT Drug Descriptors:
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology
 canertinib: CT, clinical trial
 canertinib: DT, drug therapy
 canertinib: PD, pharmacology
 carboplatin: CT, clinical trial
 carboplatin: CB, drug combination
 carboplatin: DT, drug therapy
 cyclophosphamide: CB, drug combination
 cyclophosphamide: DT, drug therapy
 cytarabine: CB, drug combination
 cytarabine: DT, drug therapy
 doxorubicin: CT, clinical trial
 doxorubicin: CB, drug combination
 doxorubicin: DT, drug therapy
 emd 55900
 erlotinib: CT, clinical trial
 erlotinib: DT, drug therapy
 erlotinib: PD, pharmacology
 etoposide: CB, drug combination
 etoposide: DT, drug therapy
 fluorouracil: CT, clinical trial
 fluorouracil: CB, drug combination
 fluorouracil: DT, drug therapy
 gefitinib: CT, clinical trial
 gefitinib: CB, drug combination
 gefitinib: DT, drug therapy
 gefitinib: PD, pharmacology
 gemcitabine: CT, clinical trial
 gemcitabine: CB, drug combination
 gemcitabine: DT, drug therapy
 homoharringtonine: CT, clinical trial
 homoharringtonine: CB, drug combination
 homoharringtonine: DT, drug therapy
 humv 833: CT, clinical trial
 humv 833: DT, drug therapy
 humv 833: PD, pharmacology
 hydroxyurea: CB, drug combination
 hydroxyurea: DT, drug therapy
 imatinib: CT, clinical trial
 imatinib: CB, drug combination
 imatinib: DT, drug therapy
 imatinib: PD, pharmacology
 interferon: CT, clinical trial
 interferon: CB, drug combination
 interferon: DT, drug therapy
 irinotecan: CT, clinical trial
 irinotecan: CB, drug combination
 irinotecan: DT, drug therapy
 oxaliplatin: CT, clinical trial
 oxaliplatin: CB, drug combination
 oxaliplatin: DT, drug therapy
 paclitaxel: CT, clinical trial
 paclitaxel: CB, drug combination
 paclitaxel: DT, drug therapy

pelitinib: CT, clinical trial
 pelitinib: DT, drug therapy
 pelitinib: PD, pharmacology
 phthalazine derivative: CT, clinical trial
 phthalazine derivative: DT, drug therapy
 phthalazine derivative: PD, pharmacology
 *protein tyrosine kinase inhibitor: CT, clinical trial
 *protein tyrosine kinase inhibitor: CB, drug combination
 *protein tyrosine kinase inhibitor: DT, drug therapy
 *protein tyrosine kinase inhibitor: PD, pharmacology
 quinazoline derivative: CT, clinical trial
 quinazoline derivative: DT, drug therapy
 quinazoline derivative: PD, pharmacology
 semaxanib: CT, clinical trial
 semaxanib: CB, drug combination
 semaxanib: DT, drug therapy
 semaxanib: PD, pharmacology
 sorafenib: CT, clinical trial
 sorafenib: DT, drug therapy
 sorafenib: PD, pharmacology
 taxane derivative: CT, clinical trial
 taxane derivative: CB, drug combination
 taxane derivative: DT, drug therapy
 trastuzumab: CT, clinical trial
 trastuzumab: CB, drug combination
 trastuzumab: DT, drug therapy
 unclassified drug
 unindexed drug
 vandetanib: CT, clinical trial
 vandetanib: DT, drug therapy
 vandetanib: PD, pharmacology

RN (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid)
 252916-29-3; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3;
 (carboplatin) 41575-94-4; (cyclophosphamide) 50-18-0; (cytarabine)
 147-94-4, 69-74-9; (doxorubicin) 23214-92-8, 25316-40-9; (erlotinib)
 183319-69-9, 183321-74-6; (etoposide) 33419-42-0; (fluorouracil) 51-21-8;
 (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (gemcitabine)
 103882-84-4; (homoharringtonine) 26833-87-4; (hydroxyurea) 127-07-1;
 (imatinib) 152459-95-5, 220127-57-1; (irinotecan) 100286-90-6;
 (oxaliplatin) 61825-94-3; (paclitaxel) 33069-62-4; (pelitinib)
 257933-82-7; (semaxanib) 186610-95-7; (sorafenib) 284461-73-0;
 (trastuzumab) 180288-69-1; (vandetanib) 338992-00-0, 338992-48-6,
 443913-73-3
 CN bay 43 9006; ci 1033; ekb 569; emd 55900; humv 833; iressa; osi 774; sti
 571; su 5416; su 6668; zd 1839; zd 6474

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ACCESSION NUMBER: 2003471818 EMBASE Full-text
 TITLE: Pharmacogenetic candidate genes for melanoma.
 AUTHOR: Hull, Christopher; Leachman, Sancy (correspondence)
 CORPORATE SOURCE: Department of Dermatology, Univ. of Utah School of
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 @hci.utah.edu
 AUTHOR: Larson, April; Leachman, Sancy (correspondence)
 CORPORATE SOURCE: Huntsman Cancer Institute, Salt Lake City, UT, United
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 SOURCE: Pharmacogenomics, (Nov 2003) Vol. 4, No. 6, pp. 753-765.
 Refs: 140
 ISSN: 1462-2416 CODEN: PARMFL

COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 013 Dermatology and Venereology
 016 Cancer
 022 Human Genetics
 037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 4 Dec 2003

Last Updated on STN: 4 Dec 2003

AB The incidence of melanoma is rising at an alarming rate and has become an important public health concern. If detected early, melanoma carries an excellent prognosis after appropriate surgical resection. Unfortunately, advanced melanoma has a poor prognosis and is notoriously resistant to radiation and chemotherapy. The relative resistance of melanoma to a wide-range of chemotherapeutic agents and high toxicity of current therapies has prompted a search for effective alternative treatments that would improve prognosis and limit side effects. Advances in molecular genetics are revealing in increasing detail the mechanisms responsible for the development of melanoma. Hopefully, elucidation of these pathways will provide a means of screening high-risk individuals and allow new drug development for prevention and treatment by identification of specific pharmacological targets. This review will summarize the genetics of melanoma with the goal of providing insights into potential pharmacogenetic candidate genes.

CT Medical Descriptors:
 adverse drug reaction
 cancer chemotherapy
 cancer incidence
 cancer prevention
 cancer radiotherapy
 cancer screening
 cancer surgery
 drug targeting
 high risk patient
 human
 *melanoma: DI, diagnosis
 *melanoma: DT, drug therapy
 *melanoma: ET, etiology
 *melanoma: PC, prevention
 *melanoma: SU, surgery
 molecular genetics
 nonhuman
 *pharmacogenetics
 prognosis
 public health
 retrospective study
 review
 skin carcinogenesis

CT Drug Descriptors:
 5 aza 2' deoxycytidine: DT, drug therapy
 7 hydroxystaurosporine: DT, drug therapy
 7 hydroxystaurosporine: PD, pharmacology
 ARF protein: EC, endogenous compound
 cyclin dependent kinase inhibitor: PD, pharmacology
 flavopiridol: DT, drug therapy
 flavopiridol: PD, pharmacology
 helix loop helix protein: EC, endogenous compound
 imatinib: PD, pharmacology
 melanocortin 1 receptor: EC, endogenous compound
 phosphatidylinositol 3,4,5 trisphosphate 3 phosphatase: EC, endogenous

compound
 protein farnesyltransferase inhibitor: PD, pharmacology
 protein inhibitor: PD, pharmacology
 protein inhibitor: TP, topical drug administration
 protein p16
 protein p53: EC, endogenous compound
 protein tyrosine kinase inhibitor: PD, pharmacology
 Raf protein: EC, endogenous compound
 Ras protein: EC, endogenous compound
 roscovitine: DT, drug therapy
 roscovitine: PD, pharmacology
 sorafenib: PD, pharmacology
 unclassified drug

RN (5 aza 2' deoxycytidine) 2353-33-5; (7 hydroxystaurosporine) 112953-11-4;
 (flavopiridol) 131740-09-5, 146426-40-6; (imatinib) 152459-95-5,
 220127-57-1; (melanocortin 1 receptor) 234764-00-2, 234764-02-4;
 (roscovitine) 186692-46-6; (sorafenib) 284461-73-0
 CN (1) gleevec; bay 439006
 CO (1) Novartis; Aventis; Cyclacel; Kyowa Hakko Kogyo

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ACCESSION NUMBER: 2003437254 EMBASE Full-text
 TITLE: Targeting HIF-1 for cancer therapy.
 AUTHOR: Semenza, Gregg L. (correspondence)
 CORPORATE SOURCE: McKusick-Nathans Inst. Genetic Med., Johns Hopkins University, School of Medicine, Baltimore, MD 21287-3914, United States. gsemenza@jhmi.edu
 SOURCE: Nature Reviews Cancer, (Oct 2003) Vol. 3, No. 10, pp. 721-732.
 Refs: 107
 ISSN: 1474-175X CODEN: NRCAC4
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 016 Cancer
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 13 Nov 2003
 Last Updated on STN: 13 Nov 2003

AB Hypoxia-inducible factor 1 (HIF-1) activates the transcription of genes that are involved in crucial aspects of cancer biology, including angiogenesis, cell survival, glucose metabolism and invasion. Intratumoral hypoxia and genetic alterations can lead to HIF-1 α overexpression, which has been associated with increased patient mortality in several cancer types. In preclinical studies, inhibition of HIF-1 activity has marked effects on tumour growth. Efforts are underway to identify inhibitors of HIF-1 and to test their efficacy as anticancer therapeutics.

CT Medical Descriptors:
 angiogenesis
 cell invasion
 cell proliferation
 cell survival
 clinical trial
 drug efficacy
 *drug targeting
 enzyme activation
 gene activity
 gene expression

gene function
 gene mutation
 gene overexpression
 *gene targeting
 genetic transcription
 glucose metabolism
 human
 hypoxia
 metastasis
 nonhuman
 oncogene
 oncogene neu
 priority journal
 protein binding
 protein degradation
 protein modification
 *protein targeting
 review
 signal transduction
 tissue oxygenation
 transcription regulation
 treatment failure
 tumor growth

CT Drug Descriptors:

1 benzyl 3 (5 hydroxymethyl 2 furyl)indazole: PD, pharmacology
 1 methylpropyl 2 imidazolyl disulfide: PD, pharmacology
 17 allylaminogeldanamycin: CT, clinical trial
 17 allylaminogeldanamycin: PD, pharmacology
 2 (2 amino 3 methoxyphenyl)chromone: PD, pharmacology
 2 methoxyestradiol: CT, clinical trial
 2 methoxyestradiol: PD, pharmacology
 antineoplastic agent: CT, clinical trial
 antineoplastic agent: PD, pharmacology
 camptothecin: PD, pharmacology
 celecoxib: CT, clinical trial
 celecoxib: PD, pharmacology
 erlotinib: CT, clinical trial
 erlotinib: PD, pharmacology
 G protein coupled receptor: EC, endogenous compound
 gefitinib: CT, clinical trial
 gefitinib: PD, pharmacology
 *hypoxia inducible factor 1: EC, endogenous compound
 hypoxia inducible factor 1alpha: EC, endogenous compound
 imatinib: PD, pharmacology
 mitogen activated protein kinase: EC, endogenous compound
 phosphatidylinositol 3 kinase: EC, endogenous compound
 pleurotin: PD, pharmacology
 protein tyrosine kinase inhibitor: PD, pharmacology
 sorafenib: CT, clinical trial
 sorafenib: PD, pharmacology
 temsirolimus: CT, clinical trial
 temsirolimus: PD, pharmacology
 topotecan: PD, pharmacology
 trastuzumab: PD, pharmacology
 ubiquitin protein ligase: EC, endogenous compound
 unclassified drug

RN (1 benzyl 3 (5 hydroxymethyl 2 furyl)indazole) 170632-47-0; (2 (2 amino 3 methoxyphenyl)chromone) 167869-21-8; (2 methoxyestradiol) 362-07-2; (camptothecin) 7689-03-4; (celecoxib) 169590-42-5; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6,

184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (mitogen activated protein kinase) 142243-02-5; (phosphatidylinositol 3 kinase) 115926-52-8; (sorafenib) 284461-73-0; (temsirolimus) 162635-04-3, 343261-52-9; (topotecan) 119413-54-6, 123948-87-8; (trastuzumab) 180288-69-1; (ubiquitin protein ligase) 134549-57-8
 CN bay 439006; cci 779; glivec; herceptin; iressa; osi 774; pd 98059; yc 1; zd 1839

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ACCESSION NUMBER: 2004088284 EMBASE Full-text
 TITLE: Targeted therapy for epithelial ovarian cancer: Current status and future prospects.
 AUTHOR: See, H.T. (correspondence); Kavanagh, John J.; Hu, W.; Bast Jr., R.C.
 CORPORATE SOURCE: Dept. of Gynecol. Medical Oncology, Univ. TX M. D. Anderson Cancer Ctr., Houston, TX, United States. jkavanag@mdanderson.org
 AUTHOR: Kavanagh, John J.
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 AUTHOR: See, H.T. (correspondence)
 CORPORATE SOURCE: Dept. of Gynecologic Med. Oncology, MD Anderson Cancer Center, Box 401, 1515, Holcombe Boulevard, Houston, TX 77030, United States.
 SOURCE: International Journal of Gynecological Cancer, (Nov 2003) Vol. 13, No. 6, pp. 701-734.
 Refs: 268
 ISSN: 1048-891X CODEN: IJGCEN
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 010 Obstetrics and Gynecology
 016 Cancer
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 11 Mar 2004
 Last Updated on STN: 11 Mar 2004

AB Despite advances in surgery and chemotherapy, less than 20% of patients with stage III or IV ovarian cancer survive long-term. In the past, cytotoxic regimens have been developed empirically, combining active agents at maximally tolerated doses, often without a clear rationale for their interaction. Advances in understanding the biology of ovarian cancer have identified multiple molecular targets that differ in normal and malignant cells. Targets include cell cycle regulators, growth factor receptors, signal transduction pathways, molecules that confer drug resistance, and angiogenic mechanisms. A number of targeted agents have entered clinical trials. Small molecular weight inhibitors, monoclonal antibodies, and antisense and gene therapy are all being evaluated alone and in combination with cytotoxic drugs. In contrast to earlier studies, the impact of each agent on the designated target can be assessed and agents can be matched to the genotype and phenotype of malignant and normal cells. In the long run, this should facilitate individualization of more effective, less toxic therapy for women with ovarian cancer.

CT Medical Descriptors:
 abdominal cramp: SI, side effect
 acne: SI, side effect

*angiogenesis
 animal model
 anorexia: SI, side effect
 *apoptosis
 cancer combination chemotherapy
 cancer immunotherapy
 cancer survival
 cell cycle
 cell growth
 cell immortalization
 cheilitis: SI, side effect
 chemotherapy induced emesis: SI, side effect
 clinical trial
 dermatitis: ET, etiology
 diarrhea: SI, side effect
 drug approval
 drug mechanism
 *drug targeting
 enzyme activation
 epithelium cell
 fatigue: SI, side effect
 female
 *gene therapy
 growth regulation
 gynecologic cancer: DR, drug resistance
 gynecologic cancer: DT, drug therapy
 gynecologic cancer: ET, etiology
 human
 human cell
 hypertension: SI, side effect
 interstitial lung disease: SI, side effect
 major clinical study
 meta analysis
 metastasis: CO, complication
 mouse
 multicenter study
 multidrug resistance
 myalgia: SI, side effect
 nausea: SI, side effect
 neurotoxicity: SI, side effect
 neutropenia: SI, side effect
 nonhuman
 oncogene
 oncogene neu
 *ovary cancer: DR, drug resistance
 *ovary cancer: DT, drug therapy
 *ovary cancer: ET, etiology
 phase 1 clinical trial
 phase 2 clinical trial
 phase 3 clinical trial
 priority journal
 proteinuria: SI, side effect
 pruritus: SI, side effect
 rash: SI, side effect
 review
 sensory neuropathy: SI, side effect
 signal transduction
 skin toxicity: ET, etiology
 skin toxicity: SI, side effect
 suicide gene therapy

thorax pain: SI, side effect
 thrombocytopenia: SI, side effect
 viral gene therapy
 vomiting: SI, side effect

CT

Drug Descriptors:

2 morpholino 8 phenylchromone: CB, drug combination
 2 morpholino 8 phenylchromone: DT, drug therapy
 2 morpholino 8 phenylchromone: TO, drug toxicity
 2 morpholino 8 phenylchromone: PD, pharmacology
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: AE, adverse drug reaction
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: AD, drug administration
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PO, oral drug administration
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology
 5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: AE, adverse drug reaction
 5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: CT, clinical trial
 5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: AD, drug administration
 5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: DT, drug therapy
 5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: PO, oral drug administration
 5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: PD, pharmacology
 *antineoplastic agent: AE, adverse drug reaction
 *antineoplastic agent: CT, clinical trial
 *antineoplastic agent: AD, drug administration
 *antineoplastic agent: CB, drug combination
 *antineoplastic agent: CM, drug comparison
 *antineoplastic agent: DO, drug dose
 *antineoplastic agent: IT, drug interaction
 *antineoplastic agent: DT, drug therapy
 *antineoplastic agent: TO, drug toxicity
 *antineoplastic agent: IP, intraperitoneal drug administration
 *antineoplastic agent: IV, intravenous drug administration
 *antineoplastic agent: PO, oral drug administration
 *antineoplastic agent: PK, pharmacokinetics
 *antineoplastic agent: PD, pharmacology
 antisense oligonucleotide
 atrasentan: AE, adverse drug reaction
 atrasentan: CT, clinical trial
 atrasentan: AD, drug administration
 atrasentan: DT, drug therapy
 atrasentan: IP, intraperitoneal drug administration
 atrasentan: PD, pharmacology
 bevacizumab: AE, adverse drug reaction
 bevacizumab: CT, clinical trial
 bevacizumab: AD, drug administration
 bevacizumab: DT, drug therapy
 bevacizumab: IV, intravenous drug administration
 bevacizumab: PD, pharmacology

bortezomib: AE, adverse drug reaction
bortezomib: CT, clinical trial
bortezomib: CB, drug combination
bortezomib: DO, drug dose
bortezomib: DT, drug therapy
bortezomib: PD, pharmacology
*canfosfamide: CT, clinical trial
*canfosfamide: AD, drug administration
*canfosfamide: CB, drug combination
*canfosfamide: DO, drug dose
*canfosfamide: DT, drug therapy
*canfosfamide: IV, intravenous drug administration
*canfosfamide: PD, pharmacology
cetuximab: CT, clinical trial
cetuximab: CB, drug combination
cetuximab: IT, drug interaction
cetuximab: DT, drug therapy
cetuximab: PD, pharmacology
cgp 69846a: CT, clinical trial
cgp 69846a: DT, drug therapy
cgp 69846a: PD, pharmacology
cisplatin: AE, adverse drug reaction
cisplatin: CT, clinical trial
cisplatin: CB, drug combination
cisplatin: CM, drug comparison
cisplatin: DT, drug therapy
epidermal growth factor receptor
erlotinib: AE, adverse drug reaction
erlotinib: CT, clinical trial
erlotinib: AD, drug administration
erlotinib: CM, drug comparison
erlotinib: DT, drug therapy
erlotinib: PO, oral drug administration
erlotinib: PK, pharmacokinetics
erlotinib: PD, pharmacology
gefitinib: AE, adverse drug reaction
gefitinib: CT, clinical trial
gefitinib: AD, drug administration
gefitinib: DT, drug therapy
gefitinib: PO, oral drug administration
gefitinib: PD, pharmacology
imatinib: CT, clinical trial
imatinib: DT, drug therapy
imatinib: PD, pharmacology
isi 3521
isis 3521: AE, adverse drug reaction
isis 3521: CT, clinical trial
isis 3521: DO, drug dose
isis 3521: DT, drug therapy
isis 3521: PD, pharmacology
*ispinesib: CT, clinical trial
*ispinesib: DT, drug therapy
*ispinesib: PD, pharmacology
*monoclonal antibody: AE, adverse drug reaction
*monoclonal antibody: CT, clinical trial
*monoclonal antibody: AD, drug administration
*monoclonal antibody: CB, drug combination
*monoclonal antibody: IT, drug interaction
*monoclonal antibody: DT, drug therapy
*monoclonal antibody: IV, intravenous drug administration

*monoclonal antibody: PD, pharmacology
 ONYX 015
 peginterferon: CT, clinical trial
 peginterferon: CB, drug combination
 peginterferon: IT, drug interaction
 peginterferon: DT, drug therapy
 protein kinase C inhibitor: AE, adverse drug reaction
 protein kinase C inhibitor: CT, clinical trial
 protein kinase C inhibitor: DO, drug dose
 protein kinase C inhibitor: DT, drug therapy
 protein kinase C inhibitor: PD, pharmacology
 protein tyrosine kinase inhibitor: CT, clinical trial
 protein tyrosine kinase inhibitor: AD, drug administration
 protein tyrosine kinase inhibitor: DT, drug therapy
 protein tyrosine kinase inhibitor: PO, oral drug administration
 protein tyrosine kinase inhibitor: PK, pharmacokinetics
 protein tyrosine kinase inhibitor: PD, pharmacology
 *sorafenib: AE, adverse drug reaction
 *sorafenib: CT, clinical trial
 *sorafenib: AD, drug administration
 *sorafenib: DT, drug therapy
 *sorafenib: PO, oral drug administration
 *sorafenib: PK, pharmacokinetics
 *sorafenib: PD, pharmacology
 tamoxifen: CT, clinical trial
 tamoxifen: CM, drug comparison
 tamoxifen: DT, drug therapy
 tanomastat: CT, clinical trial
 tanomastat: DT, drug therapy
 tanomastat: PD, pharmacology
 thalidomide: CT, clinical trial
 thalidomide: CM, drug comparison
 thalidomide: DT, drug therapy
 tipifarnib: AE, adverse drug reaction
 tipifarnib: CT, clinical trial
 tipifarnib: AD, drug administration
 tipifarnib: DT, drug therapy
 tipifarnib: PO, oral drug administration
 tipifarnib: PD, pharmacology
 trastuzumab: CT, clinical trial
 trastuzumab: CB, drug combination
 trastuzumab: IT, drug interaction
 trastuzumab: DT, drug therapy
 trastuzumab: PD, pharmacology
 unclassified drug
 unindexed drug
 vatalanib: AD, drug administration
 vatalanib: DT, drug therapy
 vatalanib: PO, oral drug administration
 vatalanib: PK, pharmacokinetics
 vatalanib: PD, pharmacology
 virus vector

RN (2 morpholino 8 phenylchromone) 154447-36-6; (2,4 dimethyl 5 (2 oxo 1h
 indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (5 amino 1 [3,5
 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide)
 99519-84-3; (atrasentan) 173864-34-1, 173937-91-2, 195733-43-8;
 (bevacizumab) 216974-75-3; (bortezomib) 179324-69-7, 197730-97-5;
 (canfosfamide) 158382-37-7, 439943-59-6; (cetuximab) 205923-56-4; (cgp
 69846a) 177075-18-2; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2;
 (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2,

184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (isis 3521) 151879-73-1; (ispinesib) 336113-53-2, 514820-03-2; (sorafenib) 284461-73-0; (tamoxifen) 10540-29-1; (tanomastat) 179545-76-7, 179545-77-8; (thalidomide) 50-35-1; (tipifarnib) 192185-72-1; (trastuzumab) 180288-69-1; (vatalanib) 212141-54-3, 212142-18-2

CN (1) avastin; (2) erbitux; (3) gleevec; (4) herceptin; (5) imc c225; (6) iressa; (7) ONYX 015; (8) osi 774; (9) ps 341; (10) r 115777; (11) sti 571; (12) tarceva; (13) tlk 286; (14) velcade; (15) zarnestra; (16) zd 1839; bay 12 9566; bay 43 9006; isi 3521; isis 5132; ly 294002; ptk 787; sb 715992; su 6668

CO (1) Genentech (United States); (2) Imclone (United States); (3) Novartis (Switzerland); (4) Genentech (United States); (5) Imclone (United States); (6) Astra Zeneca (United Kingdom); (7) Onyx (United States); (8) Osi (United States); (9) Millennium Pharmaceuticals (United States); (10) Johnson and Johnson (United States); (11) Novartis (Switzerland); (12) Osi (United States); (13) Telik (United States); (14) Millennium Pharmaceuticals (United States); (15) Johnson and Johnson (United States); (16) Astra Zeneca (United Kingdom)

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ACCESSION NUMBER: 2003481481 EMBASE Full-text
 TITLE: The impact of anti-angiogenic agents on cancer therapy.
 AUTHOR: Marme, Dieter (correspondence)
 CORPORATE SOURCE: Tumor Biology Center, Institute of Molecular Oncology, Breisacherstrasse 117, 79106 Freiburg, Germany. marme@tumor.bio.uni-freiburg.de
 SOURCE: Journal of Cancer Research and Clinical Oncology, (Nov 2003) Vol. 129, No. 11, pp. 607-620.
 Refs: 89
 ISSN: 0171-5216 CODEN: JCROD7
 COUNTRY: Germany
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 016 Cancer
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 ENTRY DATE: Entered STN: 29 Dec 2003
 Last Updated on STN: 29 Dec 2003

CT Medical Descriptors:
 angiogenesis
 breast cancer: DT, drug therapy
 *cancer: DT, drug therapy
 *cancer chemotherapy
 cancer combination chemotherapy
 cancer inhibition
 cancer model
 cell transformation
 clinical trial
 colorectal cancer: DT, drug therapy
 drug effect
 drug efficacy
 drug mechanism
 drug potency
 drug safety
 drug targeting
 drug tolerability
 endothelium cell
 glioblastoma: DT, drug therapy

human
 IC 50
 kidney carcinoma: DT, drug therapy
 leukemia: DT, drug therapy
 liver metastasis: CO, complication
 liver metastasis: DT, drug therapy
 lung hemorrhage: SI, side effect
 lung non small cell cancer: DT, drug therapy
 melanoma: DT, drug therapy
 nonhodgkin lymphoma: DT, drug therapy
 nonhuman
 oncogene
 pancreas cancer: DT, drug therapy
 priority journal
 protein family
 radioimmunotherapy
 regulatory mechanism
 review
 side effect: SI, side effect
 signal transduction
 stem cell
 tumor growth
 tumor suppressor gene
 tumor vascularization

CT Drug Descriptors:

2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: AE, adverse drug reaction
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology
 4 (4 fluoro 2 methyl 5 indolyloxy) 6 methoxy 7 [3 (1 pyrrolidinyl)propoxy]quinazoline: CT, clinical trial
 4 (4 fluoro 2 methyl 5 indolyloxy) 6 methoxy 7 [3 (1 pyrrolidinyl)propoxy]quinazoline: DT, drug therapy
 4 (4 fluoro 2 methyl 5 indolyloxy) 6 methoxy 7 [3 (1 pyrrolidinyl)propoxy]quinazoline: PD, pharmacology
 5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one
 5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one dimethylglycine ester: CT, clinical trial
 5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one dimethylglycine ester: DT, drug therapy
 5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one dimethylglycine ester: PO, oral drug administration
 5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one dimethylglycine ester: PD, pharmacology
 a 422885 66
 aal 993
 ag 13925
 alpha2b interferon: CB, drug combination
 alpha2b interferon: DT, drug therapy
 alpha2b interferon: PD, pharmacology
 *angiogenesis inhibitor: AE, adverse drug reaction

*angiogenesis inhibitor: CT, clinical trial
 *angiogenesis inhibitor: CB, drug combination
 *angiogenesis inhibitor: CM, drug comparison
 *angiogenesis inhibitor: DO, drug dose
 *angiogenesis inhibitor: DT, drug therapy
 *angiogenesis inhibitor: PO, oral drug administration
 *angiogenesis inhibitor: PK, pharmacokinetics
 *angiogenesis inhibitor: PD, pharmacology
 angiozyme: CT, clinical trial
 angiozyme: CB, drug combination
 angiozyme: DT, drug therapy
 angiozyme: PD, pharmacology
 antineoplastic agent: AE, adverse drug reaction
 antineoplastic agent: CT, clinical trial
 antineoplastic agent: CB, drug combination
 antineoplastic agent: CM, drug comparison
 antineoplastic agent: DO, drug dose
 antineoplastic agent: DT, drug therapy
 antineoplastic agent: PO, oral drug administration
 antineoplastic agent: PD, pharmacology
 axitinib: CT, clinical trial
 axitinib: CB, drug combination
 axitinib: DT, drug therapy
 axitinib: PD, pharmacology
 bevacizumab: AE, adverse drug reaction
 bevacizumab: CT, clinical trial
 bevacizumab: CB, drug combination
 bevacizumab: DT, drug therapy
 bevacizumab: PD, pharmacology
 bsf 466895
 carbazole derivative: CT, clinical trial
 carbazole derivative: DT, drug therapy
 carbazole derivative: PO, oral drug administration
 carbazole derivative: PD, pharmacology
 cetuximab
 chir 258
 cilengitide: AE, adverse drug reaction
 cilengitide: CT, clinical trial
 cilengitide: DO, drug dose
 cilengitide: DT, drug therapy
 cilengitide: PK, pharmacokinetics
 cilengitide: PD, pharmacology
 cnt 095
 cp 547 632: AE, adverse drug reaction
 cp 547 632: CT, clinical trial
 cp 547 632: DT, drug therapy
 cp 547 632: PD, pharmacology
 docetaxel: CB, drug combination
 docetaxel: DT, drug therapy
 docetaxel: PD, pharmacology
 e 7080
 emd 7200
 erlotinib
 gefitinib: DT, drug therapy
 gefitinib: PD, pharmacology
 gw 2286
 gw 654652
 imatinib
 imc 1c11
 isis 3521

isothiazole derivative: AE, adverse drug reaction
 isothiazole derivative: CT, clinical trial
 isothiazole derivative: DT, drug therapy
 isothiazole derivative: PD, pharmacology
 krn 633
 l 19
 ll 4
 midostaurin
 monoclonal antibody DC101: CT, clinical trial
 monoclonal antibody DC101: DT, drug therapy
 monoclonal antibody DC101: PD, pharmacology
 monoclonal antibody IMC 1C11: CT, clinical trial
 monoclonal antibody IMC 1C11: DT, drug therapy
 monoclonal antibody IMC 1C11: PD, pharmacology
 monoclonal antibody lm 609: CT, clinical trial
 monoclonal antibody lm 609: DT, drug therapy
 monoclonal antibody lm 609: PD, pharmacology
 n acetylcolchinel phosphate
 pd 166285
 PD 173074
 protein tyrosine kinase inhibitor: AE, adverse drug reaction
 protein tyrosine kinase inhibitor: CT, clinical trial
 protein tyrosine kinase inhibitor: CB, drug combination
 protein tyrosine kinase inhibitor: CM, drug comparison
 protein tyrosine kinase inhibitor: DO, drug dose
 protein tyrosine kinase inhibitor: DT, drug therapy
 protein tyrosine kinase inhibitor: PO, oral drug administration
 protein tyrosine kinase inhibitor: PD, pharmacology
 receptor antibody: CT, clinical trial
 receptor antibody: DT, drug therapy
 receptor antibody: PD, pharmacology
 rwj 417975
 sorafenib
 su 11657
 sunitinib: CT, clinical trial
 sunitinib: DT, drug therapy
 sunitinib: PD, pharmacology
 temozolomide: CM, drug comparison
 temozolomide: DT, drug therapy
 temozolomide: PD, pharmacology
 trastuzumab: DT, drug therapy
 trastuzumab: PD, pharmacology
 unclassified drug
 unindexed drug
 vandetanib: CT, clinical trial
 vandetanib: DT, drug therapy
 vandetanib: PD, pharmacology
 vasculotropin antibody: CM, drug comparison
 vasculotropin antibody: DT, drug therapy
 vasculotropin antibody: PD, pharmacology
 vasculotropin receptor 2 antibody: CT, clinical trial
 vasculotropin receptor 2 antibody: DT, drug therapy
 vasculotropin receptor 2 antibody: PD, pharmacology
 vasculotropin receptor 2 inhibitor: AE, adverse drug reaction
 vasculotropin receptor 2 inhibitor: CT, clinical trial
 vasculotropin receptor 2 inhibitor: DT, drug therapy
 vasculotropin receptor 2 inhibitor: PO, oral drug administration
 vasculotropin receptor 2 inhibitor: PD, pharmacology
 vasculotropin trap: CT, clinical trial
 vasculotropin trap: CM, drug comparison

vasculotropin trap: DT, drug therapy
 vasculotropin trap: PK, pharmacokinetics
 vasculotropin trap: PD, pharmacology
 vatalanib: CT, clinical trial
 vatalanib: CB, drug combination
 vatalanib: DO, drug dose
 vatalanib: DT, drug therapy
 vatalanib: PD, pharmacology
 zk 260 255

- RN (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (alpha2b interferon) 99210-65-8; (axitinib) 319460-85-0; (bevacizumab) 216974-75-3; (cetuximab) 205923-56-4; (cilengitide) 188968-51-6; (docetaxel) 114977-28-5; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (gw 2286) 601517-74-2; (imatinib) 152459-95-5, 220127-57-1; (isis 3521) 151879-73-1; (midostaurin) 120685-11-2; (n acetylcolchicol phosphate) 219923-05-4; (sorafenib) 284461-73-0; (sunitinib) 341031-54-7, 557795-19-4; (temozolomide) 85622-93-1; (trastuzumab) 180288-69-1; (vandetanib) 338992-00-0, 338992-48-6, 443913-73-3; (vatalanib) 212141-54-3, 212142-18-2
- CN (1) a 422885 66; (2) aal 993; (3) ag 013736; (4) ag 13925; (5) azd 2171; (6) azd 6474; (7) bay 43 9006; (8) bsf 466895; (9) cep 7055; (10) cep 7055; (11) chir 258; (12) cnt 095; (13) cp 547 632; (14) e 7080; (15) emd 121974; (16) emd 7200; (17) emd 7200; (18) gleevec; (19) gw 2286; (20) gw 654652; (21) herceptin; (22) imc 1c11; (23) imc c225; (24) iressa; (25) isis 3521; (26) isis 3521; (27) krn 633; (28) l 19; (29) ll 4; (30) pd 166285; (31) PD 173074; (32) pkc 412; (33) ptk 787; (34) ptk 787; (35) rwj 417975; (36) su 11248; (37) su 11657; (38) su 6668; (39) tarceva; (40) tarceva; (41) tarceva; (42) tsu 68; (43) vitaxin; (44) zd 6126; (45) zk 222584; (46) zk 222584; (47) zk 260 255; cep 5214
- CO (1) Abbott (United States); (2) Novartis; (3) Pfizer (United States); (4) Agouron (United States); (5) Astra Zeneca (United Kingdom); (6) Astra Zeneca (United Kingdom); (7) Bayer (United States); (8) Abbott (United States); (9) Cephalon (United States); (10) Sanofi Synthelabo (France); (11) Chiron (United States); (12) Centocor (United States); (13) Pfizer (United States); (14) Eisai (Japan); (15) Merck (Denmark); (16) Bms (United States); (17) Merck (Denmark); (18) Novartis; (19) Glaxo Wellcome (United States); (20) Glaxo SmithKline (United States); (21) Genentech; (22) Glaxo SmithKline (United States); (23) Imclone (United States); (24) Astra Zeneca (United Kingdom); (25) Isis (United States); (26) Novartis; (27) Kirin (Japan); (28) university of zurich; (29) University College London (United Kingdom); (30) Pfizer (United States); (31) Pfizer (United States); (32) Novartis; (33) Novartis (Germany); (34) Schering (Germany); (35) RW Johnson (United States); (36) Sugen (United States); (37) Sugen (United States); (38) Sugen (United States); (39) Genentech (United States); (40) Hoffmann La Roche; (41) Osi (United States); (42) Taiko (Japan); (43) Medimmune (United States); (44) Astra Zeneca (United Kingdom); (45) Novartis (Germany); (46) Schering (Germany); (47) Novartis; albert einstein (United States); Bristol Myers Squibb (United States); indiana university (United States); Oxigene (United States); peregrine (United States); Regeneron (United States); Ribozyme Pharmaceuticals (United States); scribbs clinic (United States)

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ACCESSION NUMBER: 2003500287 EMBASE Full-text
 TITLE: Highlights of the 39th Annual Meeting of the American Society of Clinical Oncology.
 AUTHOR: Prescott, Lawrence M.
 SOURCE: P and T, (Aug 2003) Vol. 28, No. 8, pp. 528-531.

ISSN: 1052-1372 CODEN: PPTTEK
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
 FILE SEGMENT: 016 Cancer
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 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 29 Dec 2003
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- AB More than 25,000 oncologists, research scientists, cancer nurses, and other health care professionals from around the world gathered at the 39th Annual Meeting of the American Society of Clinical Oncology, held in Chicago, Illinois, from May 31 to June 3, 2003, to hear the latest developments in the epidemiology, prevention, diagnosis, and treatment of a variety of cancers. The most recent studies included novel therapeutic combinations and new chemotherapeutic and biological agents for the treatment of metastatic breast cancer, bronchoalveolar cell carcinoma, pancreatic cancer, colorectal cancer, melanoma, and hematologic malignancies as well as advances in the management of chemotherapy-induced adverse effects.
- CT Medical Descriptors:
 advanced cancer: DT, drug therapy
 *anemia: DT, drug therapy
 *anemia: SI, side effect
 bone marrow toxicity: SI, side effect
 breast cancer: DT, drug therapy
 *cancer: DT, drug therapy
 *cancer chemotherapy
 cancer combination chemotherapy
 *cancer immunotherapy
 cancer survival
 chemotherapy induced emesis: SI, side effect
 chronic lymphatic leukemia: DT, drug therapy
 clinical trial
 colorectal cancer: DT, drug therapy
 conference paper
 diarrhea: SI, side effect
 drug efficacy
 drug safety
 febrile neutropenia: SI, side effect
 fever: SI, side effect
 human
 lung alveolus cell carcinoma: DT, drug therapy
 lymphadenopathy: SI, side effect
 major clinical study
 melanoma: DT, drug therapy
 metastasis: CO, complication
 metastasis: DT, drug therapy
 multicenter study
 nausea: SI, side effect
 neuropathy: SI, side effect
 neutropenia: SI, side effect
 nonhodgkin lymphoma: DT, drug therapy
 pancreas cancer: DT, drug therapy
 phase 1 clinical trial
 phase 2 clinical trial
 side effect: SI, side effect
 skin toxicity: SI, side effect

treatment outcome

vomiting: SI, side effect

CT Drug Descriptors:

*antineoplastic agent: AE, adverse drug reaction
 *antineoplastic agent: CT, clinical trial
 *antineoplastic agent: AD, drug administration
 *antineoplastic agent: CB, drug combination
 *antineoplastic agent: CM, drug comparison
 *antineoplastic agent: DO, drug dose
 *antineoplastic agent: DT, drug therapy
 *antineoplastic agent: IV, intravenous drug administration
 *antineoplastic agent: PO, oral drug administration
 *cancer vaccine: AE, adverse drug reaction
 *cancer vaccine: CT, clinical trial
 *cancer vaccine: AD, drug administration
 *cancer vaccine: DT, drug therapy
 *cancer vaccine: DL, intradermal drug administration
 *cancer vaccine: PR, pharmaceuticals
 *cancer vaccine: SC, subcutaneous drug administration
 carboplatin: AE, adverse drug reaction
 carboplatin: CT, clinical trial
 carboplatin: CB, drug combination
 carboplatin: DO, drug dose
 carboplatin: DT, drug therapy
 carcinoembryonic antigen
 cetuximab: CT, clinical trial
 cetuximab: CB, drug combination
 cetuximab: CM, drug comparison
 cetuximab: DT, drug therapy
 cyclophosphamide: AE, adverse drug reaction
 cyclophosphamide: CT, clinical trial
 cyclophosphamide: CB, drug combination
 cyclophosphamide: DT, drug therapy
 docetaxel: AE, adverse drug reaction
 docetaxel: CT, clinical trial
 docetaxel: CB, drug combination
 docetaxel: DT, drug therapy
 doxorubicin: AE, adverse drug reaction
 doxorubicin: CT, clinical trial
 doxorubicin: CB, drug combination
 doxorubicin: DT, drug therapy
 *erlotinib: CT, clinical trial
 *erlotinib: DT, drug therapy
 fludarabine: CT, clinical trial
 fludarabine: CB, drug combination
 fludarabine: DT, drug therapy
 fludarabine phosphate
 fluorouracil: AE, adverse drug reaction
 fluorouracil: CT, clinical trial
 fluorouracil: CB, drug combination
 fluorouracil: DO, drug dose
 fluorouracil: DT, drug therapy
 fluorouracil: IV, intravenous drug administration
 folfirinox: AE, adverse drug reaction
 folfirinox: CT, clinical trial
 folfirinox: DO, drug dose
 folfirinox: DT, drug therapy
 folfirinox: IV, intravenous drug administration
 granulocyte macrophage colony stimulating factor
 irinotecan: AE, adverse drug reaction

irinotecan: CT, clinical trial
 irinotecan: CB, drug combination
 irinotecan: CM, drug comparison
 irinotecan: DO, drug dose
 irinotecan: DT, drug therapy
 irinotecan: IV, intravenous drug administration
 *monoclonal antibody: AE, adverse drug reaction
 *monoclonal antibody: CT, clinical trial
 *monoclonal antibody: CB, drug combination
 *monoclonal antibody: CM, drug comparison
 *monoclonal antibody: DT, drug therapy
 nevsar
 novel erythropoiesis stimulating protein: CT, clinical trial
 novel erythropoiesis stimulating protein: CM, drug comparison
 novel erythropoiesis stimulating protein: DO, drug dose
 novel erythropoiesis stimulating protein: DT, drug therapy
 oblimersen: AE, adverse drug reaction
 oblimersen: CT, clinical trial
 oblimersen: CB, drug combination
 oblimersen: DT, drug therapy
 oblimersen: PD, pharmacology
 oxaliplatin: AE, adverse drug reaction
 oxaliplatin: CT, clinical trial
 oxaliplatin: CB, drug combination
 oxaliplatin: DO, drug dose
 oxaliplatin: DT, drug therapy
 oxaliplatin: IV, intravenous drug administration
 paclitaxel: AE, adverse drug reaction
 paclitaxel: CT, clinical trial
 paclitaxel: CB, drug combination
 paclitaxel: DO, drug dose
 paclitaxel: DT, drug therapy
 prednisone: AE, adverse drug reaction
 prednisone: CT, clinical trial
 prednisone: CB, drug combination
 prednisone: DT, drug therapy
 protein bcl 2
 protein kinase inhibitor: AE, adverse drug reaction
 protein kinase inhibitor: CT, clinical trial
 protein kinase inhibitor: AD, drug administration
 protein kinase inhibitor: CB, drug combination
 protein kinase inhibitor: DO, drug dose
 protein kinase inhibitor: DT, drug therapy
 protein kinase inhibitor: PO, oral drug administration
 protein kinase inhibitor: PD, pharmacology
 protein tyrosine kinase inhibitor: CT, clinical trial
 protein tyrosine kinase inhibitor: DT, drug therapy
 Raf protein
 recombinant erythropoietin: CT, clinical trial
 recombinant erythropoietin: CM, drug comparison
 recombinant erythropoietin: DT, drug therapy
 rituximab: AE, adverse drug reaction
 rituximab: CT, clinical trial
 rituximab: CB, drug combination
 rituximab: DT, drug therapy
 *sorafenib: AE, adverse drug reaction
 *sorafenib: CT, clinical trial
 *sorafenib: AD, drug administration
 *sorafenib: CB, drug combination
 *sorafenib: DO, drug dose

*sorafenib: DT, drug therapy
 *sorafenib: PO, oral drug administration
 *sorafenib: PD, pharmacology
 trastuzumab: AE, adverse drug reaction
 trastuzumab: CT, clinical trial
 trastuzumab: CB, drug combination
 trastuzumab: DT, drug therapy
 TRICOM vaccine
 unclassified drug
 unindexed drug
 vincristine: AE, adverse drug reaction
 vincristine: CT, clinical trial
 vincristine: CB, drug combination
 vincristine: DT, drug therapy

RN (carboplatin) 41575-94-4; (cetuximab) 205923-56-4; (cyclophosphamide) 50-18-0; (docetaxel) 114977-28-5; (doxorubicin) 23214-92-8, 25316-40-9; (erlotinib) 183319-69-9, 183321-74-6; (fludarabine phosphate) 75607-67-9; (fludarabine) 21679-14-1; (fluorouracil) 51-21-8; (irinotecan) 100286-90-6; (oblimersen) 190977-41-4; (oxaliplatin) 61825-94-3; (paclitaxel) 33069-62-4; (prednisone) 53-03-2; (protein bcl 2) 219306-68-0; (recombinant erythropoietin) 113427-24-0, 122312-54-3, 130455-76-4; (rituximab) 174722-31-7; (sorafenib) 284461-73-0; (trastuzumab) 180288-69-1; (vincristine) 57-22-7

CN (1) aranesp; (2) bay 43 9006; (3) camptosar; (4) eloxatin; (5) erbitux; (6) erbitux; (7) fludara; (8) genasense; (9) herceptin; (10) paraplalin; (11) procrit; (12) rituxan; (13) rituxan; (14) tarceva; (15) taxol; (16) taxotere; (17) TRICOM vaccine; cytoxan; endoxan; nevsar

CO (1) Amgen; (2) Bayer; (3) Pharmacia; (4) Sanofi Synthelabo; (5) Imclone; (6) Merck; (7) Berlex; (8) Genta; (9) Genentech; (10) Bristol Myers Squibb; (11) Ortho; (12) Genentech; (13) Idec; (14) Genentech; (15) Bristol Myers Squibb; (16) Aventis; (17) Therion

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ACCESSION NUMBER: 2003156049 EMBASE Full-text
 TITLE: Signal transduction modulators for cancer therapy: From promise to practice?
 AUTHOR: Lobbezoo, Marinus W., Dr. (correspondence); Van Kalken, Coenraad
 CORPORATE SOURCE: NDDO Research Foundation, Amsterdam, Netherlands. lobbezoo@euronet.nl
 AUTHOR: Giaccone, Giuseppe
 CORPORATE SOURCE: VU Medical Center, Amsterdam, Netherlands.
 SOURCE: Oncologist, (2003) Vol. 8, No. 2, pp. 210-213.
 Refs: 3
 ISSN: 1083-7159 CODEN: OCOLF6
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
 FILE SEGMENT: 016 Cancer
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 ENTRY DATE: Entered STN: 9 May 2003
 Last Updated on STN: 9 May 2003

CT Medical Descriptors:
 cancer: DT, drug therapy
 *cancer chemotherapy
 clinical trial
 conference paper

drug approval
 drug design
 drug screening
 drug targeting
 food and drug administration
 human
 priority journal
 side effect: SI, side effect
 *signal transduction

CT Drug Descriptors:
 1,4 diamino 1,4 bis(2 aminophenylthio) 2,3 dicyanobutadiene
 17 allylamino 17 demethoxygeldanamycin: DV, drug development
 2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: DV, drug development
 4 [6 methoxy 7 [3 (1 piperidinyl)propoxy] 4 quinazolinyl] 1
 piperazinecarboxylic acid (4 isopropoxyphenyl)amide: DV, drug development
 6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine
 7 hydroxystaurosporine
 *antineoplastic agent: AE, adverse drug reaction
 *antineoplastic agent: CT, clinical trial
 *antineoplastic agent: CB, drug combination
 *antineoplastic agent: DV, drug development
 *antineoplastic agent: DT, drug therapy
 *antineoplastic agent: PO, oral drug administration
 *antineoplastic agent: PD, pharmacology
 ap23451: DV, drug development
 bevacizumab: CT, clinical trial
 bevacizumab: CB, drug combination
 bevacizumab: DV, drug development
 bevacizumab: DT, drug therapy
 bevacizumab: PD, pharmacology
 bortezomib
 canertinib: DV, drug development
 cetuximab: DV, drug development
 cpd 5: DV, drug development
 ct 32228: DV, drug development
 erlotinib: AE, adverse drug reaction
 erlotinib: CT, clinical trial
 erlotinib: DV, drug development
 erlotinib: DT, drug therapy
 erlotinib: PD, pharmacology
 flavopiridol: DV, drug development
 gefitinib: AE, adverse drug reaction
 gefitinib: CT, clinical trial
 gefitinib: DV, drug development
 gefitinib: DT, drug therapy
 gefitinib: PD, pharmacology
 gw 211: DV, drug development
 imatinib: DV, drug development
 imc 1c11: DV, drug development
 imc 2c6: DV, drug development
 imc ic11
 matuzumab: DV, drug development
 n acetylcolchinol phosphate
 pertuzumab: DV, drug development
 protein tyrosine kinase
 semaxanib: DV, drug development
 signal transduction modulator: AE, adverse drug reaction
 signal transduction modulator: CT, clinical trial

signal transduction modulator: CB, drug combination
 signal transduction modulator: DV, drug development
 signal transduction modulator: DT, drug therapy
 signal transduction modulator: PO, oral drug administration
 signal transduction modulator: PD, pharmacology
 sorafenib: DV, drug development
 sunitinib: CT, clinical trial
 sunitinib: DV, drug development
 sunitinib: DT, drug therapy
 sunitinib: PO, oral drug administration
 sunitinib: PD, pharmacology
 temsirolimus: DV, drug development
 tipifarnib: DV, drug development
 trastuzumab: DV, drug development
 unclassified drug
 unindexed drug
 vandetanib

RN (1,4 diamino 1,4 bis(2 aminophenylthio) 2,3 dicyanobutadiene) 109511-58-2;
 (2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide)
 212631-79-3; (7 hydroxystaurosporine) 112953-11-4; (bevacizumab)
 216974-75-3; (bortezomib) 179324-69-7, 197730-97-5; (canertinib)
 267243-28-7, 289499-45-2, 338796-35-3; (cetuximab) 205923-56-4;
 (erlotinib) 183319-69-9, 183321-74-6; (flavopiridol) 131740-09-5,
 146426-40-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (imatinib)
 152459-95-5, 220127-57-1; (matuzumab) 339186-68-4; (n acetylcolchinol
 phosphate) 219923-05-4; (protein tyrosine kinase)
 80449-02-1; (semaxanib) 186610-95-7; (sorafenib) 284461-73-0;
 (sunitinib) 341031-54-7, 557795-19-4; (temsirolimus) 162635-04-3,
 343261-52-9; (tipifarnib) 192185-72-1; (trastuzumab) 180288-69-1;
 (vandetanib) 338992-00-0, 338992-48-6, 443913-73-3
 CN ap23451; bay 43 9006; c225; cci 779; ci 1033; ci 1040; cpd 5; ct 32228; ct
 53518; emd 72000; gw 211; imc 2c6; imc ic11; osi 774; pki 166; ps 341;
 r115777; st1571; sul1248; su5416; u0126; ucn 01; zd1839; zd6126; zd6474

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ACCESSION NUMBER: 2003436243 EMBASE Full-text
 TITLE: The pipeline of new anticancer agents for breast cancer
 treatment in 2003.
 AUTHOR: Awada, A. (correspondence); Cardoso, F.; Atalay, G.;
 Giuliani, R.; Mano, M.; Piccart, M.J.
 CORPORATE SOURCE: Jules Bordet Institute, Chemotherapy Unit, Boulevard de
 Waterloo 125, 1000 Brussels, Belgium. ahmad.awada@bordet.be
 SOURCE: Critical Reviews in Oncology/Hematology, (Oct 2003) Vol.
 48, No. 1, pp. 45-63.
 Refs: 172
 ISSN: 1040-8428 CODEN: CCRHEC
 COUNTRY: Ireland
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 016 Cancer
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 13 Nov 2003
 Last Updated on STN: 13 Nov 2003

AB In recent years, strategy in cancer therapy in general, and breast cancer in
 particular, has been the use of maximum tolerated doses of toxic non-specific
 agents as well as the investigation of a range of new agents that specifically

target tumor-related molecules, in a variety of biological pathways. The trial of chemotherapy (CT) versus chemotherapy+trastuzumab (Herceptin®) in HER-2-overexpressing metastatic breast cancer (MBC) was one of the first to use a biological agent in combination with chemotherapy with success and, together with some trials of taxanes in anthracycline-resistance patients one of the few to demonstrate an overall survival (OS) advantage in MBC. Five main molecular pathways are of particular interest in terms of new drug development in breast cancer: the estrogen receptor (ER) pathway, the tyrosine kinase signal transduction pathway, the cell cycle regulation pathway, the apoptosis pathway and the angiogenesis pathway. This review will focus on new agents, cytotoxic, hormonal and molecular-targeted, which are in advanced clinical stages of development for the treatment of MBC. .COPYRGT. 2003 Elsevier Ireland Ltd. All rights reserved.

CT Medical Descriptors:
alopecia: SI, side effect
anemia: SI, side effect
angiogenesis
anorexia: SI, side effect
antineoplastic activity
apoptosis
arthralgia: SI, side effect
asthenia: SI, side effect
blood toxicity: SI, side effect
*breast cancer: DR, drug resistance
*breast cancer: DT, drug therapy
cancer chemotherapy
cancer survival
cardiotoxicity: SI, side effect
cell cycle
chemotherapy induced emesis: SI, side effect
clinical trial
congestive heart failure: SI, side effect
constipation: SI, side effect
diarrhea: SI, side effect
drug effect
drug efficacy
drug eruption: SI, side effect
drug targeting
fatigue: SI, side effect
febrile neutropenia: SI, side effect
gastrointestinal symptom: SI, side effect
gene therapy
hand foot syndrome: SI, side effect
human
leukopenia: SI, side effect
metastasis: DT, drug therapy
mucosa inflammation: SI, side effect
myalgia: SI, side effect
nausea: SI, side effect
neuropathy: SI, side effect
neurotoxicity: SI, side effect
neutropenia: SI, side effect
peripheral neuropathy: SI, side effect
review
sensory neuropathy: SI, side effect
side effect: SI, side effect
signal transduction
stomatitis: SI, side effect
thrombocytopenia: SI, side effect
transaminitis: SI, side effect

CT Drug Descriptors:

3 (4 amino 1,3 dihydro 1,3 dioxo 2h isoindol 2 yl)glutarimide
 angiogenesis inhibitor: DT, drug therapy
 angiogenesis inhibitor: PD, pharmacology
 anthracycline derivative: AE, adverse drug reaction
 anthracycline derivative: CT, clinical trial
 anthracycline derivative: CB, drug combination
 anthracycline derivative: CM, drug comparison
 anthracycline derivative: DT, drug therapy
 anthracycline derivative: PD, pharmacology
 antimetabolite: AE, adverse drug reaction
 antimetabolite: CB, drug combination
 antimetabolite: DT, drug therapy
 antimetabolite: PO, oral drug administration
 antimetabolite: PD, pharmacology
 *antineoplastic agent: AE, adverse drug reaction
 *antineoplastic agent: CT, clinical trial
 *antineoplastic agent: CB, drug combination
 *antineoplastic agent: CM, drug comparison
 *antineoplastic agent: DT, drug therapy
 *antineoplastic agent: IP, intraperitoneal drug administration
 *antineoplastic agent: TU, intratumoral drug administration
 *antineoplastic agent: PO, oral drug administration
 *antineoplastic agent: PD, pharmacology
 aromatase inhibitor: DT, drug therapy
 aromatase inhibitor: PD, pharmacology
 arzoxifene: DT, drug therapy
 arzoxifene: PD, pharmacology
 bms 184476: CT, clinical trial
 bms 184476: CM, drug comparison
 bms 184476: DT, drug therapy
 bms 184476: PD, pharmacology
 bortezomib
 canertinib
 cc 7085
 cdc 801
 cgp 69846a
 cm 101
 cyclooxygenase 2 inhibitor: CT, clinical trial
 cyclooxygenase 2 inhibitor: DT, drug therapy
 cyclooxygenase 2 inhibitor: PD, pharmacology
 cytotoxic agent: AE, adverse drug reaction
 cytotoxic agent: CT, clinical trial
 cytotoxic agent: CB, drug combination
 cytotoxic agent: CM, drug comparison
 cytotoxic agent: DT, drug therapy
 cytotoxic agent: IP, intraperitoneal drug administration
 cytotoxic agent: TU, intratumoral drug administration
 cytotoxic agent: PO, oral drug administration
 cytotoxic agent: PD, pharmacology
 DNA topoisomerase inhibitor: AE, adverse drug reaction
 DNA topoisomerase inhibitor: CT, clinical trial
 DNA topoisomerase inhibitor: DT, drug therapy
 DNA topoisomerase inhibitor: PD, pharmacology
 docetaxel: AE, adverse drug reaction
 docetaxel: CT, clinical trial
 docetaxel: CM, drug comparison
 docetaxel: DT, drug therapy
 docetaxel: PD, pharmacology
 doxorubicin

erlotinib
fulvestrant: CT, clinical trial
fulvestrant: DT, drug therapy
fulvestrant: PD, pharmacology
gefitinib: CT, clinical trial
gefitinib: DT, drug therapy
gefitinib: PD, pharmacology
ixabepilone: AE, adverse drug reaction
ixabepilone: CT, clinical trial
ixabepilone: DT, drug therapy
ixabepilone: PD, pharmacology
lapatinib
lenalidomide
letrozole: CT, clinical trial
letrozole: CM, drug comparison
letrozole: DT, drug therapy
letrozole: PD, pharmacology
lonafarnib
marimastat
navelbine: CT, clinical trial
navelbine: DT, drug therapy
navelbine: PO, oral drug administration
navelbine: PD, pharmacology
paclitaxel: AE, adverse drug reaction
paclitaxel: CT, clinical trial
paclitaxel: CM, drug comparison
paclitaxel: DT, drug therapy
paclitaxel: PD, pharmacology
paclitaxel poliglumex: CT, clinical trial
paclitaxel poliglumex: DT, drug therapy
paclitaxel poliglumex: PD, pharmacology
pemetrexed
pk 166
platinum derivative: AE, adverse drug reaction
platinum derivative: CM, drug comparison
platinum derivative: DT, drug therapy
platinum derivative: PD, pharmacology
proteasome inhibitor: CT, clinical trial
proteasome inhibitor: DT, drug therapy
proteasome inhibitor: PD, pharmacology
raloxifene: DT, drug therapy
raloxifene: PD, pharmacology
retinoid derivative: DT, drug therapy
retinoid derivative: PD, pharmacology
rpr 109881a
rpr 116258a
sorafenib
tamoxifen: CT, clinical trial
tamoxifen: CM, drug comparison
tamoxifen: DT, drug therapy
tamoxifen: PD, pharmacology
taxane derivative: CT, clinical trial
taxane derivative: CB, drug combination
taxane derivative: DT, drug therapy
taxane derivative: PD, pharmacology
temsirolimus
tipifarnib
toremifene: DT, drug therapy
toremifene: PD, pharmacology
trabectedin: AE, adverse drug reaction

trabectedin: CT, clinical trial
 trabectedin: DT, drug therapy
 trabectedin: PD, pharmacology
 trastuzumab: CT, clinical trial
 trastuzumab: DT, drug therapy
 trastuzumab: PD, pharmacology
 unclassified drug
 unindexed drug
 vinflunine: AE, adverse drug reaction
 vinflunine: CT, clinical trial
 vinflunine: DT, drug therapy
 vinflunine: PD, pharmacology

RN (3 (4 amino 1,3 dihydro 1,3 dioxo 2h isoindol 2 yl)glutarimide)
 443912-23-0; (arxoxifene) 182133-25-1, 182133-27-3; (bortezomib)
 179324-69-7, 197730-97-5; (canertinib) 267243-28-7, 289499-45-2,
 338796-35-3; (cgp 69846a) 177075-18-2; (cm 101) 188417-67-6; (docetaxel)
 114977-28-5; (doxorubicin) 23214-92-8, 25316-40-9; (erlotinib)
 183319-69-9, 183321-74-6; (fulvestrant) 129453-61-8; (gefitinib)
 184475-35-2, 184475-55-6, 184475-56-7; (ixabepilone) 219989-84-1;
 (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (lenalidomide)
 191732-72-6; (letrozole) 112809-51-5; (lonafarnib) 193275-84-2;
 (marimastat) 154039-60-8; (navelbine) 71486-22-1; (paclitaxel poliglumex)
 263351-82-2; (paclitaxel) 33069-62-4; (pemetrexed) 137281-23-3,
 150399-23-8; (raloxifene) 82640-04-8, 84449-90-1; (sorafenib)
 284461-73-0; (tamoxifen) 10540-29-1; (temsirolimus) 162635-04-3,
 343261-52-9; (tipifarnib) 192185-72-1; (toremifene) 89778-26-7;
 (trabectedin) 114899-77-3; (trastuzumab) 180288-69-1; (vinflunine)
 162652-95-1

CN abi 007; alimta; bay 439006; bb 2516; bms 184476; bms 247550; caelyx; cc
 4047; cc 5013; cc 7085; cci 779; cdc 801; ci 1033; cm 101; ct 2103; et
 743; faslodex; gw 2016; herceptin; isis 5132; myocet; osi 774; pk 166; ps
 341; r 115777; rpr 109881a; rpr 116258a; sch 66336; taxotere; zd 1839

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ACCESSION NUMBER: 2003091304 EMBASE Full-text
 TITLE: Protein kinase inhibitors from the urea class.
 AUTHOR: Dumas, Jacques (correspondence)
 CORPORATE SOURCE: Bayer Research Center, Bayer Corporation, Pharmaceutical
 Division, 400 Morgan Lane, West Haven, CT 06516, United
 States. jacques.dumas.b@bayer.com
 SOURCE: Current Opinion in Drug Discovery and Development, (Sep
 2002) Vol. 5, No. 5, pp. 718-727.
 Refs: 74
 ISSN: 1367-6733 CODEN: CODDDF
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 016 Cancer
 029 Clinical and Experimental Biochemistry
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 25 Mar 2003
 Last Updated on STN: 25 Mar 2003

AB Protein kinase inhibitors hold great potential as novel therapies for cancer
 and inflammatory disorders. While bis-aryl ureas have been reported as kinase
 inhibitors as early as 1996, a number of publications and patent applications
 appeared in the literature during the past two years. Three urea-based kinase

inhibitors are currently undergoing clinical trials. The present review summarizes available data, and provides an overview of the structure-activity relationships against a variety of kinase targets, including p38, Raf-1 and cyclin-dependent kinases.

CT Medical Descriptors:

*angiogenesis
 animal model
 antiinflammatory activity
 antineoplastic activity
 arthritis: DT, drug therapy
 cancer chemotherapy
 *cell cycle
 clinical trial
 diarrhea: SI, side effect
 drug efficacy
 drug protein binding
 drug research
 drug safety
 drug structure
 drug targeting
 *enzyme inhibition
 fatigue: SI, side effect
 human
 human cell
 inflammation
 kidney carcinoma: DT, drug therapy
 liver cell carcinoma: DT, drug therapy
 mouse
 nonhuman
 phase 1 clinical trial
 phase 2 clinical trial
 rash: SI, side effect
 review
 structure activity relation

CT Drug Descriptors:

*3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4
 isothiazolecarboxamide: CT, clinical trial
 *3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4
 isothiazolecarboxamide: AD, drug administration
 *3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4
 isothiazolecarboxamide: AN, drug analysis
 *3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4
 isothiazolecarboxamide: CR, drug concentration
 *3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4
 isothiazolecarboxamide: DV, drug development
 *3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4
 isothiazolecarboxamide: DO, drug dose
 *3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4
 isothiazolecarboxamide: DT, drug therapy
 *3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4
 isothiazolecarboxamide: PO, oral drug administration
 *3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4
 isothiazolecarboxamide: PK, pharmacokinetics
 *3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4
 isothiazolecarboxamide: PD, pharmacology
 4 [4 (4 fluorophenyl) 1 (3 phenylpropyl) 5 (4 pyridinyl) 1h imidazol 2 yl]
 3 butyn 1 ol
 5 (2,6 dichlorophenyl) 2 (2,4 difluorophenylthio)pyrimido[1,6 b]pyridazin
 6 one: DV, drug development
 antiinflammatory agent: CT, clinical trial

antiinflammatory agent: AD, drug administration
 antiinflammatory agent: AN, drug analysis
 antiinflammatory agent: DV, drug development
 antiinflammatory agent: DO, drug dose
 antiinflammatory agent: DT, drug therapy
 antiinflammatory agent: IV, intravenous drug administration
 antiinflammatory agent: PD, pharmacology
 *cyclin dependent kinase inhibitor: CT, clinical trial
 *cyclin dependent kinase inhibitor: AN, drug analysis
 *cyclin dependent kinase inhibitor: DV, drug development
 *cyclin dependent kinase inhibitor: PD, pharmacology
 *dorapimod: CT, clinical trial
 *dorapimod: AN, drug analysis
 *dorapimod: DV, drug development
 *dorapimod: DO, drug dose
 *dorapimod: DT, drug therapy
 *dorapimod: IV, intravenous drug administration
 *dorapimod: PD, pharmacology
 enzyme inhibitor: AE, adverse drug reaction
 enzyme inhibitor: CT, clinical trial
 enzyme inhibitor: AN, drug analysis
 enzyme inhibitor: CR, drug concentration
 enzyme inhibitor: DV, drug development
 enzyme inhibitor: DO, drug dose
 enzyme inhibitor: DT, drug therapy
 enzyme inhibitor: PK, pharmacokinetics
 enzyme inhibitor: PD, pharmacology
 epidermal growth factor receptor kinase
 erlotinib: CT, clinical trial
 flavopiridol: CT, clinical trial
 gefitinib: CT, clinical trial
 imatinib: CT, clinical trial
 mitogen activated protein kinase inhibitor: CT, clinical trial
 mitogen activated protein kinase inhibitor: AN, drug analysis
 mitogen activated protein kinase inhibitor: DV, drug development
 mitogen activated protein kinase inhibitor: PD, pharmacology
 *protein kinase inhibitor: AE, adverse drug reaction
 *protein kinase inhibitor: CT, clinical trial
 *protein kinase inhibitor: AD, drug administration
 *protein kinase inhibitor: AN, drug analysis
 *protein kinase inhibitor: CR, drug concentration
 *protein kinase inhibitor: DV, drug development
 *protein kinase inhibitor: DO, drug dose
 *protein kinase inhibitor: DT, drug therapy
 *protein kinase inhibitor: IV, intravenous drug administration
 *protein kinase inhibitor: PO, oral drug administration
 *protein kinase inhibitor: PK, pharmacokinetics
 *protein kinase inhibitor: PD, pharmacology
 protein tyrosine kinase inhibitor: CT, clinical trial
 protein tyrosine kinase inhibitor: AN, drug analysis
 protein tyrosine kinase inhibitor: DV, drug development
 protein tyrosine kinase inhibitor: PD, pharmacology
 quinazoline derivative: DV, drug development
 ruboxistaurin: DV, drug development
 rw 67657: DV, drug development
 *sorafenib: AE, adverse drug reaction
 *sorafenib: CT, clinical trial
 *sorafenib: AD, drug administration
 *sorafenib: AN, drug analysis
 *sorafenib: DV, drug development

*sorafenib: DO, drug dose
 *sorafenib: DT, drug therapy
 *sorafenib: PO, oral drug administration
 *sorafenib: PD, pharmacology
 unclassified drug
 *urea derivative: AE, adverse drug reaction
 *urea derivative: CT, clinical trial
 *urea derivative: AD, drug administration
 *urea derivative: AN, drug analysis
 *urea derivative: CR, drug concentration
 *urea derivative: DV, drug development
 *urea derivative: DO, drug dose
 *urea derivative: DT, drug therapy
 *urea derivative: IV, intravenous drug administration
 *urea derivative: PO, oral drug administration
 *urea derivative: PK, pharmacokinetics
 *urea derivative: PD, pharmacology

RN (3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4 isothiazolecarboxamide) 252003-65-9; (4 [4 (4 fluorophenyl) 1 (3 phenylpropyl) 5 (4 pyridinyl) 1h imidazol 2 yl] 3 butyn 1 ol) 215303-72-3; (doramapimod) 285983-48-4; (epidermal growth factor receptor kinase) 79079-06-4; (erlotinib) 183319-69-9, 183321-74-6; (flavopiridol) 131740-09-5, 146426-40-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (ruboxistaurin) 169939-93-9, 169939-94-0; (sorafenib) ~~284461-73-0~~

CN (1) bay 43 9006; (2) birb 796; (3) cp 547632; (4) ly 333531; (5) osi 774; (6) rwj 67657; (7) vx 745; (8) zd 1839; glivec

CO (1) Bayer; (2) Boehringer Ingelheim; (3) Pfizer; (4) Lilly; (5) Osi; (6) RW Johnson; (7) Vertex; (8) Astra Zeneca; Amgen; Aventis; Banyu; BASF; Glaxo SmithKline; Pharmacia Upjohn; Sugen

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ACCESSION NUMBER: 2002326813 EMBASE Full-text
 TITLE: The chemistry of biological processes: Editorial overview.
 AUTHOR: McAlpine, James (correspondence); Culver, Kenneth; Ecker, David
 CORPORATE SOURCE: Phytera Inc., 377 Plantation Street, Worcester, MA 01605, United States. aandjmcaldpine@yahoo.com
 SOURCE: Current Opinion in Drug Discovery and Development, (Mar 2002) Vol. 5, No. 2, pp. 191-193.
 ISSN: 1367-6733 CODEN: CODDFE
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; Editorial
 FILE SEGMENT: 037 Drug Literature Index
 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
 LANGUAGE: English
 ENTRY DATE: Entered STN: 3 Oct 2002
 Last Updated on STN: 3 Oct 2002

CT Medical Descriptors:
 Bifidobacterium
 Clostridium
 DNA vector
 drug activity
 *drug development
 drug screening
 editorial
 Salmonella

CT Drug Descriptors:

2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid
 3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2
 thienylsulfonyl) 1h 1,4 benzodiazepine
 6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3
 d]pyrimidine
 adl 681
 angiogenesis inhibitor
 antibiotic agent
 antineoplastic agent
 bim 46228
 canertinib
 cyclin dependent kinase inhibitor
 epidermal growth factor receptor
 erlotinib
 fluorouracil
 gefitinib
 imatinib
 lb 42908
 lonafarnib
 nl 2001
 paclitaxel
 pelitinib
 phosphotransferase inhibitor
 protein kinase C inhibitor
 protein tyrosine kinase inhibitor
 recombinant antibody
 semaxanib
 sorafenib
 tipifarnib
 unclassified drug
 unindexed drug
 vancomycin
 vandetanib
 vatalanib

- RN (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid)
 252916-29-3; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4
 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9,
 195987-41-8; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3;
 (erlotinib) 183319-69-9, 183321-74-6; (fluorouracil) 51-21-8; (gefitinib)
 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5,
 220127-57-1; (lonafarnib) 193275-84-2; (paclitaxel) 33069-62-4;
 (pelitinib) 257933-82-7; (semaxanib) 186610-95-7; (sorafenib)
~~284461-73-0~~; (tipifarnib) 192185-72-1; (vancomycin) 1404-90-6,
 1404-93-9; (vandetanib) 338992-00-0, 338992-48-6, 443913-73-3; (vatalanib)
 212141-54-3, 212142-18-2
- CN (1) adl 681; (2) bay 439006; (3) bim 46228; (4) bms 214662; (5) ci 1033;
 (6) ekb 569; (7) lb 42908; (8) nl 2001; (9) osi 774; (10) pki 166; (11)
 ptk 787; (12) r 115777; (13) sch 66336; (14) sti 571; (15) su 5416; (16)
 su 6668; (17) zd 1839; (18) zd 6474; taxol
- CO (1) Novartis; (2) Bayer; (3) Biomeasure; (4) Bristol Myers Squibb; (5)
 Pfizer; (6) Wyeth Ayerst; (7) LG Chemical; (8) Nuoncology; (9) Osi; (10)
 Novartis; (11) Novartis; (12) Janssen; (13) Schering Plough; (14) Gleevec;
 (15) Sugen; (16) Sugen; (17) Astra Zeneca; (18) Astra Zeneca

L110 ANSWER 84 OF 84 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights
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ACCESSION NUMBER: 2002194397 EMBASE Full-text

TITLE: IDdb News focus.

SOURCE: Current Drug Discovery, (2002) No. MAY, pp. 13-16.

ISSN: 1472-7463 CODEN: CDDUAI

COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; Note
 FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
 016 Cancer
 031 Arthritis and Rheumatism
 037 Drug Literature Index
 004 Microbiology: Bacteriology, Mycology, Parasitology
 and Virology
 008 Neurology and Neurosurgery
 LANGUAGE: English
 ENTRY DATE: Entered STN: 13 Jun 2002
 Last Updated on STN: 13 Jun 2002

CT Medical Descriptors:

alcoholism: DT, drug therapy
 allergic rhinitis: DT, drug therapy
 anemia: DT, drug therapy
 anxiety neurosis: DT, drug therapy
 asthma: DT, drug therapy
 bladder disease: DT, drug therapy
 *cancer: DT, drug therapy
 cataplexy: DT, drug therapy
 clinical trial
 condyloma: DT, drug therapy
 controlled study
 drug approval
 drug design
 drug indication
 drug manufacture
 drug marketing
 drug structure
 heart failure: DT, drug therapy
 human
 influenza: DT, drug therapy
 influenza: PC, prevention
 kidney cancer: DT, drug therapy
 narcolepsy: DT, drug therapy
 non insulin dependent diabetes mellitus: DT, drug therapy
 nonhodgkin lymphoma: DT, drug therapy
 nose congestion: DT, drug therapy
 note
 osteoarthritis: DT, drug therapy
 papilloma: DT, drug therapy
 patent
 rheumatoid arthritis: DT, drug therapy
 *stroke: DT, drug therapy
 thromboembolism: DT, drug therapy
 thromboembolism: PC, prevention
 *virus infection: DT, drug therapy
 Wart virus

CT Drug Descriptors:

alpha adrenergic receptor stimulating agent: CB, drug combination
 alpha adrenergic receptor stimulating agent: DT, drug therapy
 antisense oligonucleotide: CT, clinical trial
 antisense oligonucleotide: DT, drug therapy
 apoptosis inhibitor: DT, drug therapy
 arixta
 beta 3 adrenergic receptor stimulating agent: CT, clinical trial
 beta 3 adrenergic receptor stimulating agent: DT, drug therapy
 bucindolol
 camptothecin derivative: CT, clinical trial

10/590724

camptothecin derivative: DT, drug therapy
carboxylic acid derivative: DT, drug therapy
celecoxib: DT, drug therapy
chir 200131
desloratadine: DT, drug therapy
DNA: CT, clinical trial
DNA: CB, drug combination
DNA: DT, drug therapy
epi 2010
fondaparinux: DT, drug therapy
histamine H1 receptor antagonist: CB, drug combination
histamine H1 receptor antagonist: DT, drug therapy
histamine H3 receptor agonist: DT, drug therapy
influenza vaccine: CT, clinical trial
influenza vaccine: DT, drug therapy
interleukin 2 receptor antibody: CT, clinical trial
interleukin 2 receptor antibody: DT, drug therapy
krp 199
loratadine: DT, drug therapy
naltrexone derivative: CT, clinical trial
naltrexone derivative: DT, drug therapy
ori 1001
ortataxel
oxybate sodium: DT, drug therapy
oxybutynin: CT, clinical trial
oxybutynin: DT, drug therapy
oxybutynin: TD, transdermal drug administration
phosphotransferase inhibitor: CT, clinical trial
phosphotransferase inhibitor: DT, drug therapy
phosphotransferase inhibitor: PO, oral drug administration
 protein tyrosine kinase inhibitor: DV, drug development
 protein tyrosine kinase inhibitor: DT, drug therapy
recombinant erythropoietin: DV, drug development
recombinant erythropoietin: DT, drug therapy
rituximab: CT, clinical trial
rituximab: CB, drug combination
rituximab: DT, drug therapy
rosiglitazone: DT, drug therapy
sb 418790
serine proteinase inhibitor: DV, drug development
serine proteinase inhibitor: DT, drug therapy
solabegron
sorafenib
ta hpv
taxane derivative: CT, clinical trial
taxane derivative: DT, drug therapy
unclassified drug
unindexed drug
uridine derivative: CT, clinical trial
uridine derivative: DT, drug therapy
valdecoxib: DT, drug therapy
vasopressin receptor antagonist: CT, clinical trial
vasopressin receptor antagonist: DT, drug therapy
virus vaccine: CT, clinical trial
virus vaccine: DV, drug development
virus vaccine: DT, drug therapy
wk 175
wx uk 1

RN (bucindolol) 71119-11-4; (celecoxib) 169590-42-5; (desloratadine)
100643-71-8; (DNA) 9007-49-2; (fondaparinux) 104993-28-4, 114870-03-0;

(interleukin 2 receptor antibody) 179045-86-4; (loratadine) 79794-75-5;
 (ortataxel) 186348-05-0, 186348-23-2; (oxybate sodium) 502-85-2;
 (oxybutynin) 1508-65-2, 5633-20-5; (recombinant erythropoietin)
 113427-24-0, 122312-54-3, 130455-76-4; (rituximab) 174722-31-7;
 (rosiglitazone) 122320-73-4, 155141-29-0; (solabegron) 252920-94-8,
 451470-34-1; (sorafenib) 284461-73-0; (valdecoxib) 181695-72-7

CN (1) arixta; (2) arixta; (3) avandia; (4) bay 439006; (5) bextra; (6)
 bextra; (7) celebrex; (8) celebrex; (9) chir 200131; (10) clarinex; (11)
 claritin; (12) epi 2010; (13) gw 427353; (14) idn 5109; (15) krp 199; (16)
 ori 1001; (17) oxytrol; (18) rituxan; (19) sb 418790; (20) ta hpv; (21) wk
 175; (22) wx uk 1; (23) xyrem

CO (1) Organon; (2) Sanofi Synthelabo; (3) Glaxo SmithKline; (4) Bayer; (5)
 Pfizer; (6) Pharmacia; (7) Pfizer; (8) Pharmacia; (9) Chiron; (10)
 Schering Plough; (11) Schering Plough; (12) epigenesis; (13) Glaxo
 SmithKline; (14) Bayer; (15) Kyorin; (16) OriGenix Technologies; (17)
 Watson; (18) Dynavax; (19) Glaxo SmithKline; (20) Xenova; (21) Willex
 Biotechnology; (22) Willex Biotechnology; (23) Orphan

=> d his nofile

(FILE 'HOME' ENTERED AT 10:58:16 ON 16 JUL 2008)

FILE 'HCAPLUS' ENTERED AT 10:58:27 ON 16 JUL 2008

L1 1 SEA ABB=ON PLU=ON US20070142440/PN
D IBIB AB IT SC
SEL RN

FILE 'REGISTRY' ENTERED AT 10:59:13 ON 16 JUL 2008

L2 47 SEA ABB=ON PLU=ON (102-56-7/BI OR 1199-46-8/BI OR 139691-76-2
/BI OR 144697-16-5/BI OR 150027-19-3/BI OR 176977-85-8/BI OR
19438-10-9/BI OR 220000-87-3/BI OR 2835-98-5/BI OR 28443-50-7/B
I OR 349-65-5/BI OR 372092-80-3/BI OR 400-99-7/BI OR 43115-40-8
/BI OR 446-36-6/BI OR 454-81-9/BI OR 53981-24-1/BI OR 67-56-1/B
I OR 74-89-5/BI OR 771-61-9/BI OR 7719-09-7/BI OR 80449-02-1/BI
OR 827025-41-2/BI OR 827025-43-4/BI OR 856424-02-7/BI OR
864291-02-1/BI OR 864291-04-3/BI OR 864291-06-5/BI OR 864291-08
-7/BI OR 864291-10-1/BI OR 864291-12-3/BI OR 864291-14-5/BI OR
864291-16-7/BI OR 864291-18-9/BI OR 864291-20-3/BI OR 864291-22
-5/BI OR 864291-24-7/BI OR 864291-26-9/BI OR 864291-28-1/BI OR
864291-32-7/BI OR 864291-34-9/BI OR 864291-39-4/BI OR 95-03-4/B
I OR 95-55-6/BI OR 95-84-1/BI OR 98-98-6/BI OR 99-76-3/BI)

L3 STRUCTURE UPLOADED
D

L4 1 SEA SSS SAM L3
D SCAN

L5 14 SEA ABB=ON PLU=ON L2 AND 3/N

L6 0 SEA ABB=ON PLU=ON L2 AND 4/N

FILE 'STNGUIDE' ENTERED AT 11:03:11 ON 16 JUL 2008

FILE 'REGISTRY' ENTERED AT 11:04:56 ON 16 JUL 2008

L7 STRUCTURE UPLOADED
L8 SCR 2043 AND 1918
L9 3 SEA SSS SAM L7 NOT L8
L10 16 SEA ABB=ON PLU=ON L2 AND 3-9/NR
D SCAN

FILE 'STNGUIDE' ENTERED AT 11:39:41 ON 16 JUL 2008

D COST

FILE 'REGISTRY' ENTERED AT 11:50:36 ON 16 JUL 2008

L11 STRUCTURE UPLOADED
D
L12 25 SEA SSS SAM L11 NOT L8
L13 SCR 2021
L14 33 SEA SSS SAM L11 AND L13 NOT L8
L15 SCR 1995 OR 2021
L16 30 SEA SSS SAM L11 AND L15 NOT L8
L17 SCR 1841
L18 50 SEA SSS SAM L11 AND L17 NOT L8

FILE 'STNGUIDE' ENTERED AT 11:55:43 ON 16 JUL 2008

FILE 'REGISTRY' ENTERED AT 11:56:29 ON 16 JUL 2008

L19 STRUCTURE UPLOADED
D

10/590724

L20 50 SEA SSS SAM L19 NOT L8
L21 50 SEA SSS SAM L19 AND L17 NOT L8
L22 SCR 2043 AND 1918 AND 1842
L23 48 SEA SSS SAM L19 NOT L22
L24 47 SEA ABB=ON PLU=ON L2 NOT 30-99/C
L25 47 SEA ABB=ON PLU=ON L2 NOT 35-99/C

FILE 'STNGUIDE' ENTERED AT 12:06:12 ON 16 JUL 2008

FILE 'REGISTRY' ENTERED AT 12:08:16 ON 16 JUL 2008

L26 STRUCTURE UPLOADED
D
L27 50 SEA SSS SAM L26 NOT L22
L28 50 SEA SSS SAM L26 AND L15 NOT L22
L29 SCR 2043 AND 1918 AND 1842 AND 2016
L30 50 SEA SSS SAM L26 AND L15 NOT L29
L31 STRUCTURE UPLOADED
D
L32 35 SEA SSS SAM L31 NOT L22
L33 35 SEA SSS SAM L31 AND L15 NOT L22
L34 36 SEA SSS SAM L31 AND L15 NOT L29

FILE 'STNGUIDE' ENTERED AT 12:30:14 ON 16 JUL 2008

FILE 'REGISTRY' ENTERED AT 12:38:18 ON 16 JUL 2008

L35 STRUCTURE UPLOADED
L36 50 SEA SSS SAM L35 AND L15 NOT L29

FILE 'STNGUIDE' ENTERED AT 12:39:05 ON 16 JUL 2008

FILE 'REGISTRY' ENTERED AT 12:40:08 ON 16 JUL 2008

L37 STRUCTURE UPLOADED
D
L38 50 SEA SSS SAM L37 AND L15 NOT L29
L39 SCR 2043 AND 1918 AND 2050 AND 1842 AND 2016
L40 50 SEA SSS SAM L37 AND L15 NOT L39
L41 SCR 1995 OR 2021 OR 1841
L42 50 SEA SSS SAM L37 AND L41 NOT L39

FILE 'STNGUIDE' ENTERED AT 12:49:58 ON 16 JUL 2008

FILE 'STNGUIDE' ENTERED AT 12:54:24 ON 16 JUL 2008

FILE 'REGISTRY' ENTERED AT 12:54:29 ON 16 JUL 2008

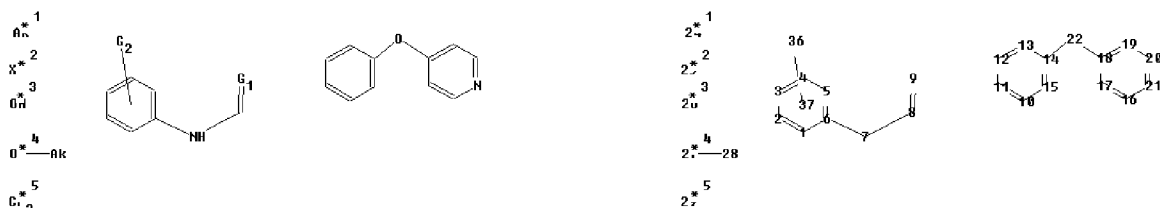
L43 STRUCTURE UPLOADED
D
L44 50 SEA SSS SAM L43 AND L41 NOT L39
L45 STRUCTURE UPLOADED
D
L46 50 SEA SSS SAM L45 AND L41 NOT L39

FILE 'STNGUIDE' ENTERED AT 13:03:34 ON 16 JUL 2008

FILE 'REGISTRY' ENTERED AT 13:17:03 ON 16 JUL 2008

L47 STRUCTURE UPLOADED
D

Uploading L11.str



chain nodes :

7 8 9 22 24 25 26 27 28 29 36

ring nodes :

1 2 3 4 5 6 10 11 12 13 14 15 16 17 18 19 20 21

chain bonds :

6-7 7-8 8-9 14-22 18-22 27-28

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21

17-18 18-19 19-20 20-21

exact/norm bonds :

6-7 7-8 8-9 14-22 18-22 27-28

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21

17-18 18-19 19-20 20-21

isolated ring systems :

containing 1 : 10 : 16 :

G1:O,S

G2:[*1],[*2],[*3],[*4],[*5]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom

11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom

20:Atom 21:Atom

22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 36:CLASS

37:Atom

L48 SCR 2043 AND 1918 AND 2050

L49 50 SEA SSS SAM L47 NOT L48

L50 1662 SEA SSS FUL L47 NOT L48

L51 14 SEA ABB=ON PLU=ON L50 AND L2

SAVE TEMP L50 NAT724REGL11/A

FILE 'HCAPLUS' ENTERED AT 13:24:34 ON 16 JUL 2008

L52 607 SEA ABB=ON PLU=ON L50

L53 584 SEA ABB=ON PLU=ON L52 AND PHARMAC?/SC,SX

L54 64 SEA ABB=ON PLU=ON L53 AND (AY<2004 OR PY<2004 OR PRY<2004)

L55 0 SEA ABB=ON PLU=ON L54 AND L1

10/590724

E TYROSINE KINASE RECEPTORS/CT

E E3+ALL

L56 2011 SEA ABB=ON PLU=ON "TYROSINE KINASE RECEPTORS"+UF/CT
L57 20 SEA ABB=ON PLU=ON L56 AND L52
L58 63 SEA ABB=ON PLU=ON L54 NOT L57
L59 334654 SEA ABB=ON PLU=ON TYROSINE KINASE? OR KINASE? OR KINASE
INHIB?
L60 3212 SEA ABB=ON PLU=ON TIE(W)2 OR TIE2 OR VEGRF OR RAF KINASE?
L61 335008 SEA ABB=ON PLU=ON L59 OR L60
L62 382 SEA ABB=ON PLU=ON L52 AND L61
L63 382 SEA ABB=ON PLU=ON L52 AND L61
L64 1797 SEA ABB=ON PLU=ON (TIE2 OR TIE(W)2 OR VEGFR OR RAF) (W)
(KINASE? OR KINASE INHIB?)
L65 114 SEA ABB=ON PLU=ON L52 AND L64
L66 52 SEA ABB=ON PLU=ON L63 AND (AY<2004 OR PY<2004 OR PRY<2004)
L67 35 SEA ABB=ON PLU=ON L65 AND (AY<2004 OR PY<2004 OR PRY<2004)
L68 31 SEA ABB=ON PLU=ON L54 NOT L67
SAVE TEMP L54 NAT724HCAP/A
L69 22 SEA ABB=ON PLU=ON BURGDORF L?/AU
L70 45 SEA ABB=ON PLU=ON BUCHSTALLER H?/AU
L71 36 SEA ABB=ON PLU=ON STIEBER F?/AU
L72 28 SEA ABB=ON PLU=ON AMENDT C?/AU
L73 202 SEA ABB=ON PLU=ON GREINER H?/AU
L74 150 SEA ABB=ON PLU=ON GRELL M?/AU
L75 38 SEA ABB=ON PLU=ON SIRRENBURG C?/AU
L76 3 SEA ABB=ON PLU=ON ZENKE K?/AU
L77 10 SEA ABB=ON PLU=ON (((L69 OR L70 OR L71 OR L72 OR L73 OR L74
OR L75 OR L76)) AND L52) OR (L1 AND L52)
L78 5 SEA ABB=ON PLU=ON L77 NOT L54
SAVE TEMP L78 NAT724HCAIN/A

FILE 'REGISTRY' ENTERED AT 13:38:42 ON 16 JUL 2008

L79 1 SEA ABB=ON PLU=ON L50 AND (MEDLINE/LC OR BIOSIS/LC OR
DRUGU/LC OR EMBASE/LC)

FILE 'MEDLINE' ENTERED AT 13:39:09 ON 16 JUL 2008

L80 0 SEA ABB=ON PLU=ON L79

FILE 'BIOSIS' ENTERED AT 13:39:15 ON 16 JUL 2008

L81 89 SEA ABB=ON PLU=ON L79
L82 34 SEA ABB=ON PLU=ON L81 AND L64
L83 3 SEA ABB=ON PLU=ON L82 AND (PREP? OR SYNTHES?)
D TI 1-3
L84 0 SEA ABB=ON PLU=ON L82 AND ANGIOGENESIS INHIB?
L85 6 SEA ABB=ON PLU=ON L82 AND TYROSINE KINASE?
L86 8 SEA ABB=ON PLU=ON L83 OR L85

FILE 'DRUGU' ENTERED AT 13:42:12 ON 16 JUL 2008

L87 0 SEA ABB=ON PLU=ON L79

FILE 'EMBASE' ENTERED AT 13:42:27 ON 16 JUL 2008

L88 2050 SEA ABB=ON PLU=ON L79
L89 605 SEA ABB=ON PLU=ON L88 AND TYROSINE KINASE?
L90 1 SEA ABB=ON PLU=ON L88 AND TYROSIN KINASE INHIB?
L91 165 SEA ABB=ON PLU=ON L88 AND L64
L92 1332 SEA ABB=ON PLU=ON RAF KINASE?
L93 164 SEA ABB=ON PLU=ON L92 AND L88
D TI L90
L94 26 SEA ABB=ON PLU=ON L89 AND (PREPARAT? OR SYNTHES?)
D TI KWIC 1-4

10/590724

L95 26 SEA ABB=ON PLU=ON L94 AND (PHARMAC? OR THERAP?)
L96 27 SEA ABB=ON PLU=ON L90 OR L94
L97 0 SEA ABB=ON PLU=ON L96 AND (AY<2004 OR PY<2004 OR PRY<2004)
L98 12 SEA ABB=ON PLU=ON L89 AND (AY<2004 OR PY<2004 OR PRY<2004)

FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 13:48:43 ON 16 JUL 2008

L99 0 SEA ABB=ON PLU=ON BURGDORF LARS/AU
L100 9 SEA ABB=ON PLU=ON BUCHSTALLER HANS PETER/AU
L101 8 SEA ABB=ON PLU=ON STIEBER FRANK/AU
L102 7 SEA ABB=ON PLU=ON AMENDT CHRISTIANE/AU
L103 14 SEA ABB=ON PLU=ON GREINER HARTMUT/AU
L104 70 SEA ABB=ON PLU=ON GRELL MATTHIAS/AU
L105 19 SEA ABB=ON PLU=ON SIRRENBURG CHRISTIAN/AU
L106 2 SEA ABB=ON PLU=ON ZENKE FRANK/AU
L107 3 SEA ABB=ON PLU=ON ((L100 OR L101 OR L102 OR L103 OR L104 OR
 L105 OR L106)) AND TYROSINE KINASE?
L108 0 SEA ABB=ON PLU=ON ((L100 OR L101 OR L102 OR L103 OR L104 OR
 L105 OR L106)) AND L64

FILE 'STNGUIDE' ENTERED AT 13:52:17 ON 16 JUL 2008

D COST
D QUE L78
D QUE L107

FILE 'HCAPLUS, MEDLINE, EMBASE' ENTERED AT 13:53:35 ON 16 JUL 2008

L109 8 DUP REM L78 L107 (0 DUPLICATES REMOVED)
 ANSWERS '1-5' FROM FILE HCAPLUS
 ANSWERS '6-7' FROM FILE MEDLINE
 ANSWER '8' FROM FILE EMBASE
D L109 1-5 IBIB ABS
D L109 6-8 IBIB AB
D QUE L54
D QUE L86
D QUE L98

FILE 'HCAPLUS, BIOSIS, EMBASE' ENTERED AT 13:54:57 ON 16 JUL 2008

L110 84 DUP REM L54 L86 L98 (0 DUPLICATES REMOVED)
 ANSWERS '1-64' FROM FILE HCAPLUS
 ANSWERS '65-72' FROM FILE BIOSIS
 ANSWERS '73-84' FROM FILE EMBASE
D L110 1-64 IBIB ABS FHITSTR HITIND
D L110 65-84 IBIB AB HITIND